# Psychopharmacology Service Center Bulletin







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# *NIMH Grants for Research in Psychopharmacology*

This issue of the PSC *Bulletin* contains brief summaries of 272 projects relevant to research in psychopharmacology. Only those projects that were receiving support on January 1, 1961, are included. The summaries are based on the investigators' statements about the proposed research. Many details of the research had to be condensed or omitted, and with large, long-term programs especially, the summaries cannot reflect all the work that is under way. Other investigators who are interested in more extensive information should communicate directly with the principal investigator on the project.

The projects have been grouped into categories according to the research emphasis of the grant. As in all attempts to classify material into mutually exclusive categories, many arbitrary decisions were made. Many of the projects could also be placed under other headings.

## CLINICAL STUDIES

### *Controlled Clinical Trials of Drugs with Schizophrenic Patients*

MY–1870. **Tranquilizing Drugs in Acute Psychiatric Disorders.**

The effectiveness of reserpine and chlorpromazine in the treatment of hospitalized acutely ill psychiatric patients is being investigated in studies involving the use of a sedative and a placebo as well as the two tranquilizers. Blood pressure recordings, urinalyses, and white blood cell counts are made before and during the medication period. Patients are assessed by psychiatric residents' and nurses' observations and ratings of anxiety, sleep, appetite, etc., and by use of the Minnesota Multiphasic Personality Inventory, Purdue Pegboard, and Thematic Apperception Test.

ARTHUR J. PRANGE AND D. WILFRED ABSE, *University of North Carolina, Chapel Hill, N.C.*

MY–1983. **A Study of Ataractics in Outpatient Schizophrenics.**

This is a controlled, longitudinal investigation of the effectiveness of drug therapy (currently chlorpromazine and promazine) as a treatment for chronic schizophrenic outpatients. The major aims of the study are to determine the relationship of clinical improvement to drug therapy, to determine the quality of clinical change, to relate quality of change to the patient's intake characteristics and social milieu, and to determine the duration, stability, and quality of the effects of sustained drug therapy. The development and refinement of techniques of measuring adjustment and clinical change are of special interest. Techniques for coding such dimensions as social pathology, social role deviance, personal habits, and mood are also being developed. A large battery of tests and rating scales is being used to assess changes in psychiatric status, in specific psychological functions, and in social adjustment.

DAVID M. ENGELHARDT AND NORBERT FREEDMAN, *State University of New York, Brooklyn, N.Y.*

MY–2152. **Comparative Phenothiazine Study on Acute Admissions.**

A program of controlled clinical research has been established which is investigating the comparative effectiveness of various phenothiazine derivatives (including the newer ones as well as some which have been available for some time) in the treatment of acutely ill psychiatric patients. Both active and inactive placebos are used, and double-blind procedures are followed throughout. In addition to interest in the comparative effectiveness of the drugs, the study is also aimed at providing information on the specific indications for the use of one or another of the compounds in patients with certain types of symptomatology. Linked with the clinical studies are careful inspection of pre-admission history—with special reference to drug treatment prior to hospitalization and to the effectiveness of drug therapy in the home environment—and follow-up studies of discharged patients.

ALBERT A. KURLAND AND THOMAS E. HANLON, *Spring Grove State Hospital, Baltimore, Md.*

MY–2165. **A Study of Ataraxic Drugs with Schizophrenic Patients.**

This is a double-blind study of chlorpromazine, prochlorperazine, triflupromazine, perphenazine, an active placebo, and an inactive placebo in the treatment of chronic schizophrenic patients. Variable dosage schedules are used. Information on frequency of improvement sufficient for discharge and on social adjustment is being sought. Patient status is assessed by the Lorr Multidimensional Scale for Rating Psychiatric Patients, clinical estimates of psychiatric status, narrative clinical observations, the Minnesota Multiphasic Personality Inventory, and the Bender-Gestalt. A two-year follow-up study will make use of the Goodrich-Swengel-Saslow Revision of the Barrabee-Finesinger Scale, follow-up ques-

tionnaires, a background form, and a community receptivity scale.

DANIEL ADELSON, *California State Department of Mental Hygiene, Sacramento, Calif.*

MY–2719. **Psychotherapy of Schizophrenia.**

This research, part of a long-range program of study, is a controlled comparison of the effectiveness of the following methods of treating first-admission schizophrenic patients who have good prognoses: basic hospital care alone, and basic hospital care combined with tranquilizing drugs, electroshock therapy, or individual psychotherapy. Among the patient-assessment techniques being used are initial history, psychiatric examination, psychological tests, descriptive clinical evaluations, ratings of prognosis, the Menninger Clinic Health Sickness Rating Scale, the Lorr Multidimensional Scale for Rating Psychiatric Patients, the Clyde Mood Scale, and an "S-Sort" test to measure self-concept and self-ideal. The Goodrich-Swengel-Saslow Revision of the Barrabee-Finesinger scale will be used in the follow-up work to measure the patient's social adjustment in the community.

PHILIP R. A. MAY AND MILTON WEXLER, *Camarillo Hospital, Camarillo, Calif.*

MYP–4661. **NIMH–PSC Collaborative Study of Phenothiazines.**

This is a collaborative study in which investigators at nine different institutions are following a common research protocol. Investigators at each institution have received a grant to support their participation in the project. Their names and addresses are listed under the following grant numbers: MYP–4663, MYP–4667, MYP–4671, MYP–4673, MYP–4674, MYP–4675, MYP–4679, and MYP–4803. The following note is applicable to each of the grants.

A controlled, double-blind comparison of the efficacy of thioridazine, fluphenazine, and chlorpromazine is being carried out with acute schizophrenic patients who will be placed upon a six-week treatment regime. Improvement will be evaluated by the Lorr Inpatient Multidimensional Psychiatric Scale, the Burdock Ward Behavior Rating Scale, the Clyde Mood Scale, and by clinical judgment. Interhospital differences will be compared for drug-milieu interactions, and a large cohort of the patients will be followed up for at least one year.

MARTIN GROSS AND IRENE L. HITCHMAN, *Springfield State Hospital, Sykesville, Md.*

MYP–4663. **NIMH–PSC Collaborative Study of Phenothiazines.**

See note for grant MYP–4661.

RICHARD STEINBACH AND BERNARD I. LEVY, *Georgetown University, Washington, D.C.*

MYP–4667. **NIMH–PSC Collaborative Study of Phenothiazines.**

See note for grant MYP–4661.

KATHLEEN SMITH AND GEORGE A. ULETT, *Washington University, St. Louis, Mo.*

MYP–4671. **NIMH–PSC Collaborative Study of Phenothiazines.**

See note for grant MYP–4661.

FREDERIC F. FLACH AND CHARLES I. CELIAN, *Cornell University, New York, N.Y.*

MYP–4673. **NIMH–PSC Collaborative Study of Phenothiazines.**

See note for grant MYP–4661.

EDWIN M. DAVIDSON AND MELVIN M. KAYCE, *Boston University, Boston, Mass.*

MYP–4674. **NIMH–PSC Collaborative Study of Phenothiazines.**

See note for grant MYP–4661.

R. R. KNOWLES AND E. A. MOLES, *Kentucky State Hospital, Danville, Ky.*

MYP–4675. **NIMH–PSC Collaborative Study of Phenothiazines.**

See note for grant MYP–4661.

JOHN DONNELLY, FRANCIS J. BRACELAND, AND BERNARD C. GLUECK, JR., *Institute of Living, Hartford, Conn.*

MYP–4679. **NIMH–PSC Collaborative Study of Phenothiazines.**

See note for grant MYP–4661.

JAMES H. EWING AND HAROLD H. MORRIS, *University of Pennsylvania, Philadelphia, Pa.*

MYP–4803. **NIMH–PSC Collaborative Study of Phenothiazines.**

See note for grant MYP–4661.

GUY M. WALTERS AND CHRISTOPHER F. TERRENCE, *Rochester State Hospital, Rochester, N.Y.*

## *Controlled Clinical Trials of Drugs with Depressed Patients*

MYP–2525. **A Study of Affective Depressions.**

This is a long-term placebo-controlled investigation and comparison of the efficacy of various treatments of affective depression in hospitalized patients studied in groups categorized by age and sex (females under 40 years of age, females between 40 and 60, and males under 60). Iproniazid, isocarboxazid, imipramine, and electroconvulsive therapy will be used. An attempt will

be made to identify characteristics in the patients—from biographical and situational data as well as from psychological, biochemical, and other measures being used—which are predictive of favorable response to a given treatment. The efficacy of treatment will be investigated further in follow-up studies. Tests of cognitive and psychomotor functions, behavioral ratings, motivational and attitudinal assessments, and measures of physiological, metabolic, and biochemical functions are to be used.

J(OHN) RICHARD WITTENBORN, *Rutgers University, New Brunswick, N.J.*

MY–3314. **Drug Treatment of Hospitalized Depressed Patients.**

Three state hospitals are cooperating in this double-blind study in which depressed patients at each hospital are randomly assigned to treatment with one of several antidepressive drugs or to ECT. The latter will be used as the standard against which to test the efficacy of the drugs. The effects of treatment—measured by use of various rating scales, interviews, clinical judgment, observations of ward behavior, the Clyde Mood Scale, and follow-up studies of adjustment in the community—will be related to the social and psychiatric characteristics of the patients and to the characteristic milieu and over-all treatment program at each of the participating institutions.

MILTON GREENBLATT, *Massachusetts Mental Health Center, Boston, Mass.*, HARRY FREEMAN, *Medfield State Hospital, Medfield, Mass.*, MORRIS L. SHARP, *Westboro State Hospital, Westboro, Mass.*, AND EDWARD MESHORER, *Metropolitan State Hospital, Waltham, Mass.*

MY–3647. **MAO Inhibition and Antidepressant Correlates.**

Controlled studies, using own-control procedures as well as an independent control group, will be conducted to determine the effects of a monoamine oxidase inhibitor on the depressive syndrome in hospitalized depressed male patients. Psychiatric interviews, various psychological and psychiatric rating scales, and several physiological and biochemical measures will be used. Extent of inhibition of MAO will be determined biochemically, and an attempt will be made to correlate MAO inhibition with changes in the depressive syndrome and also with specific psychiatric areas of change.

VICTOR J. SCHENKER AND GORDON MARJERRISON, *State University of New York, Brooklyn, N.Y.*

MY–3674. **Vigilance, Sedation Threshold, Tofranil, and Depression.**

Systematic data are to be collected on the relation between psychological vigilance and sedation threshold in depressed psychotics. Sedation thresholds will be determined for normals, depressed patients, and paranoid patients who will also be given cognitive-perceptual tests related to vigilance. Hypotheses concerning the effects of impramine and electroshock therapy upon sedation threshold, vigilance, and clinical condition in depressed patients will be investigated through use of psychiatric observation and ratings, EEG studies, and a battery of psychological tests.

ALFRED S. FRIEDMAN, *Philadelphia Psychiatric Hospital, Philadelphia, Pa.*

MY–3993. **Comparative Trial of Antidepressant Drugs.**

This project is a double-blind, comparative assessment of the therapeutic and side effects of certain antidepressive drugs in hospitalized patients showing the depression syndrome. Assessment will be accomplished by clinical judgments of change, ratings of symptoms of depression, listing of side effects, body weight, blood pressure, color vision (Ishihara test), complete blood count, and serum glutamic oxalopyruvic transaminase levels. Follow-up studies of duration of therapy, transfer, and discharge will be carried out.

JOHN R. WHITTIER AND GEORGE G. HAYDU, *Creedmoor State Hospital, Queens Village, N.Y.*

## *Controlled Clinical Trials of Drugs with Neurotic Outpatients*

MY–2241. **Evaluation of Drug Therapy on Psychiatric Outpatients.**

Double-blind studies of new tranquilizers are being carried out with outpatients who show overt anxiety as a common symptom. The new drugs are compared with a "standard" drug (sedative) and a placebo. Changes in symptomatology are assessed by an adjective check list, the Funkenstein test, the Minnesota Multiphasic Personality Inventory, the Edwards Personal Preference Schedule, and psychiatrists' ratings and patients' self-ratings of severity of symptoms and adjustment. Six-month and twelve-month follow-up evaluations are to be made.

JACQUES S. GOTTLIEB AND PAUL LOWINGER, *Lafayette Clinic, Detroit, Mich.*

MY–2923. **Tranquilizers in Psychiatric Outpatient Treatment.**

A double-blind study of three tranquilizers is to be carried out with nonpsychotic psychiatric outpatients. The drug-treated groups will be compared with each other and with a group treated with psychoanalytically oriented psychotherapy, a group treated with placebo, and a group not yet receiving either drugs or psychotherapy. The patients' status will be assessed by use of the following measures before, during, and one year after treatment: therapist's judgment of changes in adjustment

status, patient's evaluation of treatment results, a Modified Barrabee-Finesinger Social Adjustment Scale, the Clyde Mood Scale, a treatment evaluation scale developed for this project, and a scale to measure the patient's self-perception of social desirability.

NORMAN Q. BRILL AND LEON EPSTEIN, *University of California, Los Angeles, Calif.*

MY–2934. **Evaluation of Drug Therapy in Psychiatric Outpatients.**

The investigation is primarily concerned with the development and improvement of methods of evaluating psychiatric drug therapy in neurotic outpatients of the type usually treated by general practitioners. A series of double-blind studies of the effects of relatively new drugs in such patients will focus special attention on methodology. Methods of evaluation will be compared, differential as opposed to gross effects of drugs will be studied, the problem of drop-out will be examined, and an attempt will be made to detect the role of such factors as transference, suggestibility, etc. Among the procedures to be used are relative and absolute measures of over-all change, the Clyde Mood Scale, the Duke Checklist, the Taylor Manifest Anxiety Scale, the Cattell Anxiety Scale, and a clinical questionnaire. The drugs to be used are tranquilizers, antidepressives, and barbiturates.

KARL RICKELS, *University of Pennsylvania, Philadelphia, Pa.*

MY–4135. **Use of Psychotherapeutic Drugs in General Practice.**

The use and value of psychopharmacological agents and other drugs in the treatment of psychoneurotic patients seen in general medical practice are being investigated by a number of general practitioners located in different parts of Great Britain. Double-blind procedures will be used to compare different drugs with one another, with placebo, and with a "standard remedy." Drug effectiveness, side effects, and long-term effects (on the patient and his family) of continued medication will be studied. Drug effects will be assessed by clinical observation. Both acute and chronic psychoneurotics will be studied. Many types of drugs will be used, tranquilizers, antidepressives, barbiturates, and stimulants.

DAVID PEARSE WHEATLEY, *General Practitioner Research Group, Twickenham, Middlesex, England.*

MYP–4731. **PSC–NIMH Outpatient Study of Drug-**
MYP–4732. **Set Interaction.**

The aims of this research are to evaluate the effectiveness of meprobamate in the treatment of neurotic outpatients, to determine the effect of patients' expectations (set) on the course of treatment, and to test the hypothesis that a "therapeutic" (i.e., positive or favorable) set potentiates response to active medication. Double-blind, placebo-controlled investigations are being carried out at three clinics simultaneously. The attitudes of the 12 participating physicians will be systematically controlled in order to influence patients' expectations. The dependent variables are patients' self-ratings and doctors' ratings on a symptom-distress check list, on the Clyde Mood Scale, and of over-all change. Drop-out will also be considered. Interclinic comparisons will be made, and an attempt will be made to validate the role behaviors of the physicians.

KARL RICKELS, *University of Pennsylvania, Philadelphia, Pa.,* AND E. H. UHLENHUTH AND L. C. PARK, *Johns Hopkins University, Baltimore, Md.*

## *Controlled Clinical Trials of Drugs with Children*

MY–2318. **Effects of Chlorpromazine on Learning in Children.**

The effects of chlorpromazine on learning and retention are being investigated in a controlled study of disturbed inpatient children. Objective measurements of learning ability, transfer of training, and retention will be carried out before, during, and after drug or placebo. The question of whether any observed effects on learning are a function of the drug's anxiety-reducing action will also be studied. Assessment procedures include paired association learning, serial learning, digit span, the Porteus Maze Test, filling in O's, tapping rate, electromyographic recordings of muscle tension in frontalis muscles, palmar galvanic skin resistance, heart rate, structured interviews, and staff ratings of anxiety level.

M. HELPER AND SOL L. GARFIELD, *University of Nebraska, Omaha, Nebr.*

MY–2583. **Drug and Cognition Studies in Disturbed Children.**

This is a series of controlled investigations designed to determine the value of various drugs in the treatment of disturbed children, delinquents, and brain-damaged children, and to identify the important variables determining the response to drug therapy. The variables being studied include diagnosis, family setting, concomitant psychotherapy, and specific attributes of the drug. Standardized methods of evaluation of parents and children are being developed. The study is also investigating cognitional processes in disturbed children and in normal controls.

LEON EISENBERG AND SONIA OSLER, *Johns Hopkins University, Baltimore, Md.*

MY–3042. **Meprobamate in Behavior Disorders with Abnormal EEG's.**

The effects of meprobamate are to be investigated in a controlled study of children who have severe behavior disorders and who exhibit abnormal EEG tracings. A

number of tests and scales are to be used in evaluating the psychological, physiological, emotional, social, and electroencephalographic effects of the drug.

DAVID R. METCALF, THOMAS T. GLASSCOCK, HAROLD W. KEELY, HAROLD NITZBERG, AND SEBASTIAN SANTOSTEFANO, *University of Colorado, Denver, Colo.*

MY–3269. **Psychopharmacology of Corticosteroids with Asthmatics.**

A double-blind study of the behavioral effects of prednisone is to be carried out with asthmatic children between the ages of 6 and 15. A battery of tests of learning (including learning and extinction of conditioned avoidance responses), psychomotor, perceptual, and cognitive functioning, and personality will be administered before, during, and after the drug-treatment period. Behavioral and certain physiological and biochemical effects are to be correlated.

KENNETH PURCELL, SAMUEL C. BUKANTZ, AND LEWIS BERNSTEIN, *Jewish National Home for Asthmatic Children, Denver, Colo.*

MY–4140. **Control of Hyperactivity in the Mentally Retarded.**

A major purpose of this project is to develop and refine a research design for evaluating the effects of drugs on behavior disorders in children. A second aspect is a double-blind, controlled study of the effects of an antidepressive drug (nialamide) on hyperactive behavior in mentally retarded, noninstitutionalized children. The hypothesis is that increased feelings of well being as a result of drug therapy should result in decreased hyperactivity and better performance. Psychological, behavioral, and sociological assessment will be made before and after treatment. The Wechsler Intelligence Scale for Children, the Minnesota Rate of Manipulation Test, Leg Persistence Test, Porteus Mazes, the Bender-Gestalt test, behavior rating scales, social worker interviews of parents (including use of the Vineland Social Maturity Scale), and evaluations of children and parents on various scales designed to measure hyperactivity, acceptance and rejection of the child, and pressure for placement of the child in an institution will be used.

SOL GORDON AND MEYER SONIS, *Philadelphia Child Guidance Clinic, Philadelphia, Pa.*, AND WARREN CHERNICK AND JOHN D. BRIDGERS, *Children's Hospital of Philadelphia, Philadelphia, Pa.*

MY–4332. **Play Patterns in Schizophrenic and Retarded Children.**

Two monographs are being prepared which will describe particular aspects of a longitudinal study of play behavior and ego function and dysfunction in normal, psychotic, and retarded children. Pharmacotherapy and psychotherapy were used in the study. The first monograph will focus on methodology, covering varieties of play behavior (especially nonverbal behavior), technical equipment, techniques of indexing ego function and play patterns, and methods, problems, and principles of observation. The second will deal with clinical and theoretical aspects of severe ego disorders in children.

EARL A. LOOMIS, JR., AND LUCILE R. MEYER, *St. Luke's Hospital, New York, N.Y.*

MY–4400. **Drugs and Psychological Functions Underlying Learning.**

The effects of hydroxyzine on learning and learning disabilities in normal and schizophrenic children are being investigated. Variables to be studied are reaction time to visual and auditory stimuli, formation and shifting of sets to patterns of visual and auditory stimuli, distinguishing and utilizing simple and complex patterns in maze learning, and the formation of conditioned responses to visual and auditory stimuli. During the period of drug administration, changes in behavior on the hospital ward, at school, and at home will be observed and compared with laboratory performances.

ALFRED M. FREEDMAN AND MARTIN DEUTSCH, *New York Medical College, New York, N.Y.*

MY–4438. **Psychopharmacological Agents in Children.**

This is a controlled study of the effects of a tranquilizer on the reading performance, social and school behavior, and perceptual and intellectual functioning in 10- to 12-year-old, intellectually normal boys with reading problems. Three treatment groups—placebo plus reading tutoring, a tranquilizer plus tutoring, tutoring without any medication—and a group given neither medication nor tutoring will be studied. The measures to be used in assessing treatment effects are the Gates Reading Test, auditory memory span, the Continuous Performance Test, the Memory for Designs Test, evaluations of classroom behavior, and social and school history.

ALFRED M. FREEDMAN AND MARTIN DEUTSCH, *New York Medical College, New York, N.Y.*

MYP–4665. **Children's Psychopharmacology Unit.**

A broad program of research is being established for the systematic study of drug treatment of hospitalized or outpatient children with various psychiatric disorders. Drugs which have been tested and found safe in the treatment of adults will be screened for effectiveness, dose range, etc., in children. Promising compounds will be studied further in controlled clinical investigations. The development and refinement of methods of objectively evaluating the efficacy of drug treatment in pediatric psychiatry will also be emphasized. Methods and tests to be used are aimed at measuring patterns of sleep and wakefulness, irritability, control of tension, apathy, vasomotor stability, activity levels, ability to concentrate and to respond to ward routine. Speech, perceptual, and

social function, and areas of development such as posture, fine coordination, and adaptive skills will also be studied. In addition, independent clinical impressions and ratings by psychiatrists, nurses, teachers, and recreation workers will be used. Follow-up studies will be carried out, and will give attention to such matters as stability of improvement and progress, value of maintenance drug therapy, and prognostic indicators.

BARBARA FISH AND ARNOLD J. FRIEDHOFF, *New York University Medical Center, New York, N.Y.*

## *Controlled Clinical Trials of Drugs with Aged Patients*

### MY–4553. **Effects of Procaine on Aged Mental Patients.**

This is a double-blind, placebo-controlled investigation of the effects of procaine (Novocain) in the treatment of geriatric patients diagnosed as either chronic brain syndrome associated with cerebral arteriosclerosis or chronic brain syndrome associated with senile brain disease. Nine courses of medication (at either of two dose levels) will be given over a 342-day period, followed by a postmedication period of 76 days. Patients on procaine and patients on placebo (saline) will be compared on clinical, neurophysiological, physiological, psychological, psychiatric, and social-behavior measures before, during, and after the medication period. The measures include physical examination, EKG, EEG, X ray, blood morphology and blood chemistry, urinalysis, neurological examination, psychological evaluation (the Graham-Kendall Memory for Designs Test, the Multidimensional Scale for Rating Psychiatric Patients, the Clyde Mood Scale, the Crownsville Check List for Evaluating Symptom Change in Psychiatric Patients, mental status, and the Minnesota Rate of Manipulation Test), and social adjustment as measured by the Hospital Adjustment Scale and by observations of ward behavior. Still photographs and sound movies are also to be made as permanent records of observations.

ARCHER C. JOHNSON, ROY J. JONES, AND JAMES I. DESHIELDS, *Crownsville State Hospital, Crownsville, Md.*

## *Early Clinical Evaluation of Drugs*

### MY–1665. **Effects of Tranquilizing Drugs on the CNS.**

This is a program of clinical psychopharmacological research which includes preliminary trials of new compounds, controlled studies of those which have shown promise of therapeutic efficacy, and studies of drug effects in normals. The drugs being studied—including tranquilizers, antidepressives, and psychotomimetics—are tested in hospitalized patients or outpatients chosen according to specific symptoms or diagnoses. Base-line laboratory tests (complete blood count, complete urinalysis, alkaline phosphatase, and cephalin flocculation) are made prior to drug treatment and at intervals thereafter. Drug effects are determined by use of clinical interviews and ratings of severity of symptoms. Parallel studies are attempting to correlate drug concentrations in the blood with clinical effects. Some of the work with normal subjects includes investigations of the blocking effects of tranquilizers in drug-induced "psychosis."

SIDNEY MALITZ, *New York State Psychiatric Institute, New York, N.Y.*

### MY–2778. **Screening Potential Stimulants on Inactive Psychotics.**

New, potentially stimulating drugs will be screened for their effects on free-operant behavior in chronic psychotics who have consistently performed at low rates of response during experiments conducted over the past few years. Drug-induced changes in behavior will be compared with detailed experimental histories which are available on these patients. The effects of various drugs, of placebo, and of no-drug conditions will be investigated in each patient. Psychiatric and psychological reevaluations will also be made periodically. Among the agents studied thus far are iproniazid, pineal extract, and ceruloplasmin.

OGDEN R. LINDSLEY, *Harvard Medical School, Boston, Mass.*

### MY–2784. **Coordinated Multiple Psychiatric Drug Screening Units.**

A systematic method of rapidly and uniformly carrying out early clinical evaluations of new psychiatric drugs is being established, and existing facilities for testing new drugs in the Nebraska hospital system are being expanded. The program consists of preliminary trials of new drugs as well as controlled studies in hospitalized chronic psychiatric patients. In some cases, a drug may be tested at two or more institutions simultaneously. Patient status is assessed by clinical observations, evaluation of mental status, descriptive check lists, a standardized form for progress notes, and a ward-observation chart.

CECIL L. WITTSON, *Nebraska Psychiatric Institute, Omaha, Nebr.*

### MY–2991. **Clinical Explorations of New Psychotropic Compounds.**

The selective effects of drugs on particular symptoms and dysfunctions are to be examined. New tranquilizers and antidepressive drugs are to be evaluated in hospitalized psychiatric patients selected for certain "target symptoms." The kind and degree of symptom changes will be evaluated on the basis of free (i.e., unstructured) observations by psychiatrists and nurses. EEG's and laboratory tests are to be made before and at intervals during treatment.

FRITZ A. FREYHAN, *Delaware State Hospital, Farnhurst, Del.*

MY–3030. **Improved Clinical Screening of Phrenotropic Drugs.**

This study is based on the premise that detailed investigation of drug effects in a few patients may be the best method of clinically screening new drugs. Methods for evaluating drug effects in small groups of patients are to be developed. Newly admitted hospital patients requiring drug treatment will be assigned to a special research ward. Carefully controlled double-blind studies of new drugs will be carried out over a three-month period for each group of patients admitted. Drug effects will be evaluated by personality and other tests, staff observations, rating scales, and laboratory data.

LEO E. HOLLISTER AND JOHN J. PRUSMACK, *Stanford University, Stanford, Calif.*

MY–3048. **Hexafluorodiethyl Ether—Its Use in Schizophrenia.**

This is an exploratory investigation of the clinical efficacy of hexafluorodiethyl ether (an inhalant convulsant) in the treatment of schizophrenia. From earlier studies the investigator has found that longer exposures to this agent not only produce convulsions but also cause coma which has an additional therapeutic effect. The aim of this study is to discover the optimal exposure and the ideal number and spacing of treatments to minimize regression and to insure beneficial effects.

ALBERT A. KURLAND, *Spring Grove State Hospital, Baltimore, Md.*

MY–3672. **Clinical Research on Psychopharmacological Drugs.**

A small full-time psychiatric research unit is being established for controlled clinical studies of drugs and for preliminary clinical studies to determine effective dose levels and dosage regimens of new drugs, the nature of therapeutic and toxic responses, type of psychopathology which responds to the drugs, etc. Data on the clinical efficacy of new compounds will be used to check the value of various animal screening techniques as predictors of drug effects in man.

MARTIN GROSS AND IRENE L. HITCHMAN, *Springfield State Hospital, Sykesville, Md.*

MY–3701. **Clinical Evaluation of New Chemotherapeutic Agents.**

A program of double-blind clinical comparisons of the effects of new psychopharmacological agents, placebo, and known drugs (e.g., chlorpromazine) in chronic schizophrenic patients is being established. Psychological tests, psychiatric interviews, and physical examinations are to be made before, during, and at the termination of treatment. Assessment of patient status will be accomplished through use of the Color Naming Test, the Comprehension subtest of the Wechsler-Bellevue, the Memory for Stories from the Wechsler Memory Scale, reaction time, tapping, the Tulane Behavior Scale, the Lorr Multidimensional Scale for Rating Psychiatric Patients, clinical interviews, and behavioral ratings.

RALPH WELLS BUDDINGTON AND ROBERT G. HEATH, *Tulane University, New Orleans, La.*

MY–3712. **Research Unit for Clinical Screening of Psychoactive Drugs.**

A research unit is being established specifically to carry out a program of pharmacological and physiological evaluations of psychopharmacological agents. Intensive clinical and laboratory studies of small groups of patients will be conducted to determine the behavioral, physiological, and biochemical actions of new drugs as well as their side effects and toxicity. Milieu factors are also to be taken into account.

WILLIAM P. BOGER, *Norristown State Hospital, Norristown, Pa.*

MYP–4669. **Controlled Drug Evaluations.**

This is a broad program of research in clinical psychopharmacology. It encompasses the development and refinement of methods for the clinical screening of psychiatric drugs, preliminary screening of new drugs, controlled clinical studies of the drugs which offer promise of being effective in the treatment of psychiatric illnesses, investigations of toxic and side effects of the drugs, and studies of the relation between toxic and therapeutic effects. A special research ward is being established which will have available for study large numbers of hospitalized patients from virtually all psychiatric diagnostic groups. Among the measures and procedures being used are the Lorr Multidimensional Scale for Rating Psychiatric Patients, laboratory profiles of blood, kidney, and liver function, independent clinical ratings, pedometer measurement of activity level, analysis of patients' vocal productions, standard occupational therapy tasks, and other techniques which may be developed or which may seem appropriate as work progresses.

ARNOLD J. FRIEDHOFF, *New York University Medical Center, New York, N.Y.*

## *Social-Psychiatric Aspects of Clinical Drug Use*

MY–1690. **Drug and Social Therapy in Chronic Schizophrenia.**

This is a follow-up study of the patients who were studied in an investigation of the effects of drugs plus "milieu" therapy in the treatment of chronic schizophrenia. In the drug-milieu study, patients were treated with or without drugs in two contrasting treatment settings, one an intensive treatment center and the other a state hospital where only routine custodial care was given. (All patients in the study were initially in the state hospital; some were transferred to the intensive treatment center for the period of the study.) The

follow-up studies now being carried out will attempt to determine the long-term effects of the different treatments on the psychiatric status and adjustment of both the discharged patients and those who are still hospitalized. Patients will be assessed by psychiatrists and social workers. Patients' families will also be interviewed.

MILTON GREENBLATT AND JULIUS LEVINE, *Massachusetts Mental Health Center, Boston, Mass.*, GEORGE W. BROOKS, *Vermont State Hospital, Waterbury, Vt.*, AND MYER ASEKOFF, *Metropolitan State Hospital, Waltham, Mass.*

MY–2535. **Home Versus Hospital Care for Schizophrenics.**

This study is designed to determine whether schizophrenics may be successfully treated at home if drug therapy is given under proper supervision. A controlled, double-blind trial will be carried out with first-admission schizophrenics given (*a*) medications at home under supervision of public health nurses, or (*b*) ordinary hospital care. The groups will be compared as to eventual rate of hospital admission and length of hospitalization, psychiatric condition, and family reactions. The following measures will be used to assess the patients: psychiatric examinations, nurses' reports and ratings, intelligence tests, objective personality tests, projective tests, interviews by social workers, and interviews of patients' families.

BENJAMIN PASAMANICK, *Columbus Psychiatric Institute and Hospital, Columbus, Ohio.*

MY–2700. **Drug Therapy in a Day-care Facility for Relapse Control.**

The aims of this study are to determine whether acutely recurring psychotic symptoms can be controlled through supervised intensive pharmacotherapy; whether patients given this form of day-care treatment can return to work more quickly than they could after hospitalization; and whether remission following day-care treatment will be as lasting as remission following hospitalization. Two main groups of relapsed or relapsing patients will be studied, those given day-care and drug therapy and those who are rehospitalized.

ELSE B. KRIS, *New York State Department of Mental Hygiene, Manhattan Aftercare Clinic, New York, N.Y.*

MY–3868. **Five-Year Community Follow-up of Discharged Patients.**

Data collected over a five-year period on three cohorts of 100 patients each will be analyzed in detail and evaluated to determine family, social, and work adjustment, need for rehospitalization, need for and tolerance of maintenance drug therapy, and other factors involved in long-term adjustment in the community. The 300 patients being studied were admitted to the Manhattan Aftercare Clinic immediately after hospital discharge and have been closely followed since that time. Data are available on the patients' psychotic symptoms, family background, family constellation, racial and ethnic background, diagnosis, religious affiliation, marital status, previous social and economic adjustment, extent to which patients have been self-supporting since hospitalization, details of maintenance drug therapy, recurrence of symptoms, and many other areas. Of special interest are the possible correlation of adjustment and length of hospitalization, the role of maintenance drug therapy, family attitudes, social factors involved in relapse, and the role of supportive psychotherapy.

ELSE B. KRIS, *New York State Department of Mental Hygiene, Manhattan Aftercare Clinic, New York, N.Y.*

MY–4030. **Hospital and Community Coordination for After-care.**

This is a study of the comparative effectiveness and feasibility of two methods of after-care for formerly hospitalized psychiatric patients who are living in an area located some 150 miles from the hospital. One method involves patient contact with an outpatient clinic which maintains a close and continuing relationship with the hospital; the second method involves the services of a social worker from the hospital who is assigned to the community in which the discharged patients are living. Both methods permit the participating staff to become acquainted with the patients and their special situations and problems during the period of hospitalization. Procedures used in the clinic will include group psychotherapy or individual therapy if indicated. Pre-admission and predischarge procedures are also being studied.

ELMER F. LOWRY, JR., *Alexandria Mental Hygiene Clinic, Alexandria, Va.*, AND JAMES B. PETTIS, *Western State Hospital, Staunton, Va.*

MY–4122. **Traits, Behavior, and Release of Mental Patients.**

This project represents an attempt to determine the association between (*a*) treatment prior to hospitalization, time of hospitalization in relation to onset of symptoms, person who had the patient hospitalized, and time of release or discharge from hospital and (*b*) any of a wide variety of social and demographic variables in cohorts of hospitalized functional psychotic patients. Possible differences between findings with cohorts of patients hospitalized before drugs were extensively used and those hospitalized since drugs have been widely used will also be examined. Data for the study are being taken from existing hospital records. Factors to be investigated include social characteristics such as education, marital status, race, sex, social habits (drinking, friends, church attendance, employment, etc.), type of person who hospitalized the patient, types of pre-admission symptoms reported, and others. Of special interest is the possibility of a relationship between any of these fac-

tors and the probability of release within a year of hospitalization.

ERWIN L. LINN, *Catholic University of America, Washington, D.C.*

MY–4253. **Psychiatric Services in an Underdeveloped Country.**

A number of exploratory studies will be carried out in a recently established acute treatment unit located in an area where very little psychiatric service is available. An underlying aim of the work is to determine whether this unit can serve as a prototype for the establishment of psychiatric treatment centers in other areas where there is a severe shortage of psychiatric service. Detailed data on psychiatric problems in Haiti will be collected and analyzed to test observations which have been made concerning the low incidence of alcoholism and psychotic depression, the high incidence of epilepsy, the usual length of hospitalization, the incidence of mental disorders in patients from different social classes and of different sexes, and other aspects of mental illness in Haiti. The work may include simple controlled studies of the effects of phenothiazines or other drugs, comparisons of acute treatment methods at this unit with those used in the United States or elsewhere, the preparation of a history of the unit, and additional training for some of the staff.

ALAIN SANSEIGNE, *Haiti Psychiatric Center, Port-au-Prince, Haiti,* AND NATHAN S. KLINE, *Rockland State Hospital, Orangeburg, N.Y.*

MY–4589. **Follow-up Study of Treatment of Schizophrenia.**

Continuing on evaluation of the effectiveness of five psychiatric treatment methods (EST, individual psychotherapy, individual psychotherapy plus tranquilizing drugs, tranquilizing drugs only, and milieu only), this study will investigate the posthospital adjustment of first-admission schizophrenics for a two-year period following discharge. Patients will be studied three months, six months, one year, and two years after discharge. Measures will include structured and interpretive sociological and social-worker interviews of a member of the patient's family, psychological tests (including the MMPI, Clyde Mood Scale, Wechsler subtests, and the Shipley Hartford Scale), semistructured psychiatric interviews, ratings on the Camarillo Dynamic Assessment Scales, the Symptom Rating Sheet, the Menninger Health Sickness Scale, and a Clyde Mood Scale sort of how the psychiatrist sees the patient.

PHILIP R. A. MAY AND ELEANOR B. SHELDON, *Camarillo Hospital, Camarillo, Calif.*

3M–9132. **A Program of Research on Mental Health in Industry.**

This is a very broad program of social-psychological research on the effects of industrial environment on mental health. One of the many aspects of the program is concerned with the use of alcohol, sedatives, tranquilizers, and other drugs.

JOHN R. P. FRENCH, JR., ROBERT L. KAHN, AND FLOYD C. MANN, *University of Michigan, Ann Arbor, Mich.*

## BASIC RESEARCH ON MECHANISMS OF DRUG ACTION

### *Psychological and Physiological Studies with Psychiatric Patients*

MY–1055. **Objectification of Verbal Behavior Analysis.**

This is a program of research which deals with the establishment of an objective method of recording and analyzing the form and content of verbal behavior. The diagnostic and psychodynamic significance of small samples of speech is being analyzed, and an attempt is being made to determine whether this method can be used as a reliable, objective means of measuring the psychological effects of drugs. Samples of speech are analyzed by grammatical criteria, language patterns, and content. Indexes derived from the analyses of verbal behavior are compared with quantitative scores derived from the Minnesota Multiphasic Personality Inventory, and psychiatric ratings. The subjects studied include normals, schizophrenics, and other types of psychiatric patients. The drugs used include phenothiazine derivatives, barbiturates, iproniazid, pipradrol, and corticosteroids.

LOUIS A. GOTTSCHALK AND GOLDINE C. GLESER, *University of Cincinnati, Cincinnati, Ohio.*

MY–1121. **Time Sense in Normal and Psychopathologic States.**

This is a long-term program of research on estimations of time by healthy, blind, mentally ill, alcoholic, and metabolically disordered subjects. The effects of various conditions, including drug treatment, on estimations of time are being investigated. The following parameters relevant to temporal judgments are being measured: subjective (social) vs. objective (clock) time estimation, psychophysical methodology, response conditions and number of response categories, step-interval anchor effects, background anchor effects, intersensory studies, and sociometric correlates, etc. The drugs employed are dextro-amphetamine, secobarbital, LSD, and placebo.

SANFORD GOLDSTONE AND WILLIAM T. LHAMON, *Baylor University College of Medicine, Houston, Tex.*

MY–1204. **Explorations in Psychopharmacology.**

This is a continuing program of research in which psychopharmacological methods are being employed in investigations aimed at clarifying a number of problems

relevant to psychopathology, psychophysiology, and psychodynamics. The effects of experimental drug states on personality and thought processes are being studied in normal and disturbed human subjects, and some work is being carried out with animals. Of special interest is the relation of neurochemical changes to psychological changes. LSD and serotonin are currently being used.

DANIEL X. FREEDMAN, *Yale University, New Haven, Conn.*

MY–1261. **Brain Metabolism in Psychiatric Disorders.**

This project deals with the interrelations between cerebral blood flow, metabolism, and clinical manifestations of mental disorders, with special attention to individual variations and to the effects of drugs on these variables. Longitudinal studies with schizophrenics and patients with organic cerebral disorders are being carried out. Senile and nonsenile elderly subjects will also be studied. Chlorpromazine and reserpine are among the drugs being used.

FRITZ A. FREYHAN, *Delaware State Hospital, Farnhurst, Del.*

MY–1281. **Autonomic Responses in Psychosomatic Disorders.**

This study is investigating the association between specific patterns of autonomic activity and reactivity and specific psychosomatic disorders. Autonomic nervous system functions of psychosomatic patients are being compared with those of healthy subjects. The effects of drug-induced changes in ANS response on recovery from, or recurrence of, psychosomatic disorders are also being studied. Among the measures being used are electrical skin resistance, skin temperature, heart rate, blood pressure, stomach motility, and personality data from psychiatric interviews and psychological tests.

M. A. WENGER, *University of California, Los Angeles, Calif.*

MY–1305. **Trace Alkaloid Metabolism in Mental Disease.**

The role of trace nitrogen metabolites in the etiology or symptomatology of schizophrenia and manic-depressive psychosis is being assessed with special reference to compounds which are formed endogenously and excreted in the urine. An attempt is being made to isolate and identify abnormal metabolites which occur in samples taken from mental patients, and to correlate urinary pattern with the mental disturbance. Incorporated in the research are a controlled study of the metabolism (particularly the demethylation) of imipramine and studies of primary, secondary, and tertiary amines in urinary extracts from patients not on drug.

HARRY GOLDENBERG, *Hillside Hospital, Glen Oaks, N.Y.*

MY–1422. **Cerebral Physiology in Functional Disorders.**

Evidence of differences in central nervous system excitability—including differences in the effects of tranquilizers—and in the organization of cerebral responses is being sought in animals, in normal human subjects, and in many types of psychotic patients. EEG response to various kinds of stimuli, the relation of response to psychiatric profiles, and neural mechanisms of different types of responses are being investigated.

HARRY H. GARNER, JAMES E. P. TOMAN, AND ROBERT F. JEANS, *Chicago Medical School, Chicago, Ill.*

MY–1434. **Biologically Inactive Catechols in Mental Disease.**

This is a continuing research on the metabolism of the catecholamines in mentally ill patients and in animals. One part of the work involves an investigation of the effects of Antabuse (an oxidative enzyme inhibitor) on amine metabolism in man. Patients administered Antabuse will be given tritiated norepinephrine and patients on maintenance Antabuse will receive tryptamine orally. Using an isotopic dilution technique, 3-methoxy-4-hydroxy-mandelic acid excretion rates will be determined in patients subjected to ECT. Metabolism of tryptamine in patients with liver disease is also being investigated.

S. BERNARD WORTIS, *New York University, New York, N.Y.*

MY–1752. **Psychomotility, Drugs, and Schizophrenic Rehabilitation.**

Combining neurological, psychiatric, and psychological approaches, the investigators are exploring ways of measuring concomitant changes in psychiatric state and psychomotor performance. The aims of this work are to delineate the relationship between the psychomotor performance of chronic schizophrenics and the rehabilitation of these patients by means of drug therapy, and to determine whether performance on a battery of psychomotor tests is predictive of the outcome of drug therapy and attempts at social rehabilitation. Follow-up studies will be carried out at various intervals after hospital discharge.

GEORGE W. BROOKS AND LELON A. WEAVER, JR., *University of Vermont, Burlington, Vt.*

MY–1971. **Attributes of Schizophrenics and Phren-**
MY–1972. **otropic Drug Action.**

This is a broad, interdisciplinary program of research on the psychological, biochemical, and physiological dimensions of schizophrenia. The long-range aims are

to differentiate schizophrenics from other types of patient groups and to delineate subtypes of schizophrenia. The relationship between the nature of the psychiatric disorder and individual patient responses to various psychiatric drugs will be analyzed. The work also includes psychopharmacological studies with animals. A wide variety of psychological, biochemical, neurophysiological, and psychiatric tests are to be used to differentiate types of patients and to assess psychiatric status following drug therapy.

RALPH W. GERARD, *University of Michigan, Ann Arbor, Mich.*, AND KENNETH B. MOORE, *Ypsilanti State Hospital, Ypsilanti, Mich.*

MY–2061. **Affects, Physiological Changes, and Humoral Levels.**

This is an investigation of the mechanisms by which emotional states produce physiological changes. Earlier studies have indicated a correlation between catecholamine levels in urine and the presence of anxiety in human subjects. A replication of these and other findings relating to humoral processes will be carried out with normals, psychiatric patients, and patients with physiological or endocrinological disorders. In a later phase of the study psychological tests will be employed to assess the role of stress on body metabolism.

SANFORD I. COHEN AND ALBERT J. SILVERMAN, *Duke University, Durham, N.C.*

MY–2244. **Comparative Effects of Ataractic Drugs.**

A number of small-scale controlled studies of the therapeutic effects of several drugs are being carried out with hospitalized psychiatric patients. Perphenazine, trifluoperazine, and a hormone-vitamin preparation for geriatric patients are among the agents being investigated. Such variables as dosage level, specificity of drug action, and staff attitudes toward drug therapy are being studied, and methods of recording psychological and physiological changes in behavior are being developed.

MILTON H. ANDERSON, *Evansville State Hospital, Evansville, Ind.*

MY–2350. **A Technique to Investigate and Predict Drug Response.**

The major purposes of this project are to determine the value of the interaction chronograph as a technique for differentiating subgroups of schizophrenics and for measuring and predicting drug effects in schizophrenics. An attempt is being made to determine whether drugs cause systematic changes in patterns of interpersonal behavior; whether drug effects on interaction chronograph measurements of interactional factors (e.g., duration of speech, number of interruptions, etc.) can be predicted; and whether there is a correlation between (*a*) clinical improvement and (*b*) improvement as reflected in activity and improvement scores taken from interaction chronograph measurements. Phenothiazines are among the drugs being used. Chronic and acute patients of various types will be studied. Findings can then be compared with available data on normal subjects.

NATHAN S. KLINE, *Rockland State Hospital, Orangeburg, N.Y.*

MY–2587. **A Study of the Long-Term Effects of Tranquilizers.**

The effects of chlorpromazine, meprobamate, and no treatment on serum protein and serum glycoprotein profiles will be compared in chronic psychiatric patients to determine the long-term physiological effects of these drugs. Electrophoretic determinations of serum proteins and serum glycoproteins, and cephalin flocculation determinations of thymol turbidity will be made. Electrophoretic values will be correlated with the findings of currently used laboratory procedures.

MICHAEL J. CARVER AND CECIL L. WITTSON, *Nebraska Psychiatric Institute, Omaha, Nebr.*

MY–2635. **Personality, Emotion, and Drug Actions.**

This is a long-term investigation of neurophysiological correlates of personality and emotion in psychiatric patients and normal subjects. Evoked EEG responses to sensory stimuli will be used in studies of the effects of drugs on cortical excitability cycles and the relationship between drug-induced individual differences in changes of cortical excitability and individual differences in personality and emotion. Among the drugs to be used are methamphetamine, LSD, amobarital, chlorpromazine, and imipramine. Affective state and personality patterns will be assessed in psychiatric interviews and by questionnaires.

CHARLES SHAGASS, *State University of Iowa, Iowa City, Iowa.*

MY–2715. **Behavior Changes With Induced Altered Brain Functions.**

This is a long-term investigation of the mode of action of psychopharmacological agents, the interrelationship of neurophysiological change and behavioral response, and the extent to which pretreatment psychological, perceptual, and neurophysiological functioning can be used to predict clinical and behavioral response to drug therapy. Double-blind studies of chronic and acute administration of a variety of drugs will be carried out with hospitalized psychotics and psychoneurotics. Patients will be evaluated by EEG's, objective and projective psychological tests, psychomotor performance, Mecholyl test responses, uptake of radioactive iodine, structured family interviews, a social-attitude scale, psychiatric observations and ratings of improvement, and analyses of language changes.

MAX FINK, *Hillside Hospital, Glen Oaks, N.Y.*

MY–2755. **Differential Learning, Diagnosis, and Drug Research.**

This is a broad program of research to establish procedures for evaluating pharmacological, physical, and psychological methods of treating psychiatric disorders. Parallel studies of drug effects on emotional and nonemotional behavior will be carried out with animals, normal human subjects, and psychiatric patients. Measures of learning will be examined with the aim of differentiating between various psychiatric diagnostic groups and controls. A learning theory differentiating between emotionally and nonemotionally mediated learning as affected by psychiatric diagnosis and treatment will be tested. Data on basal physiological activity levels will be related to measures of speed of learning and resistance to extinction. EEG analyses are being made, and one of the aims of the program is to develop and apply newer electronic methods of analyzing EEG data. Among the drugs being studied are imipramine, tranylcypromine, thioridazine, and nialamide.

GEORGE A. ULETT AND JOHN A. STERN, *Washington University, St. Louis, Mo.*

MY–2844. **Hexafluorodiethyl Ether and Convulsive Threshold.**

This investigation of the convulsant action of hexafluorodiethyl ether will attempt to localize the drug's anatomic site of action by means of EEG studies. By careful measurement of the dosage and the resultant EEG abnormalities, convulsive thresholds and patterns of EEG response will be determined in epileptics, nonepileptics, and patients who pose diagnostic problems in an attempt to establish the value of the drug as a diagnostic tool.

ALBERT A. KURLAND AND C. MARSHALL, *Spring Grove State Hospital, Baltimore, Md.*

MY–2936. **Mechanism of Action of Psychic Energizers.**

The mechanism of action of antidepressives, particularly iproniazid and iproniazid analogues, is being investigated through studies of the relation of MAO inhibition to psychiatric, behavioral, and autonomic responses to the drugs. Psychological tests, including projective techniques, are also being used. Infusions of $C^{14}$-labeled epinephrine are given before and during drug treatment as a means of determining the MAO-inhibitory activity of the drugs. The autonomic (blood pressure and pulse rate), psychiatric, and psychological effects of iproniazid analogues which have varying degrees of MAO-inhibitory activity are being compared with the effects of iproniazid in depressed schizophrenic patients. Results of studies of normals will be compared with the findings from the work with psychotic patients.

HUDSON HOAGLAND AND OSCAR RESNICK, *Worcester Foundation for Experimental Biology, Shrewsbury, Mass.*

MY–2938. **Relation of Mecholyl Test to Catecholamine Excretion.**

The aims of this investigation are to determine the effects of experimental and clinical changes on blood pressure responses to Mecholyl, and to investigate the role of epinephrine, norepinephrine, serotonin, and their metabolites in the reaction to Mecholyl. The study is being carried out in hospitalized psychiatric patients. An automatic recording sphygmomanometer, which reportedly eliminates subjective factors and gives a more accurate basal blood pressure, will be used in the determination of blood pressure. Urine will be analyzed for catecholamine content. Individual variations in response will be studied in relation to subjective response and diurnal changes in clinical condition; type of response will be examined in relation to diagnosis, sex, and age.

ARNOLD B. BLUMBERG AND HARRY GOLDENBERG, *Hillside Hospital, Glen Oaks, N.Y.*

MY–3006. **Tranquilizer Withdrawal Studies in Schizophrenia.**

Psychiatric and psychological rating scales, performance tests, and biochemical and neurological investigations are being used in double-blind investigations of the effects of drug withdrawal in chronic schizophrenics being treated with phenothiazines or reserpine. Assessment procedures include mental status examinations, the Lorr Multidimensional Scale for Rating Psychiatric Patients, daily ward observations, performance on the Wechsler-Bellevue scale and Bender-Gestalt tests, investigations of hormonal and cation changes, and biochemical studies of blood and urine.

CALVIN HANNA AND GEORGE W. BROOKS, *University of Vermont, Burlington, Vt.*

MY–3031. **Effects and Mode of Action of Psychopharmaceuticals.**

The objective of this research is to determine whether there are identifiable and measurable physiological and behavioral effects of psychopharmacological agents. Detailed biochemical, endocrinological, and behavioral studies will be carried out with a few hospitalized patients who are regularly receiving reserpine, a phenothiazine derivative, or a monoamine oxidase inhibitor. The techniques to be employed include the use of radioisotopes and extensive analyses of 17-ketosteroids and corticosteroids. The correlation between metabolic and behavioral-psychosocial effects of the drugs is to be examined.

NATHAN S. KLINE, J. BLAIR, E. H. CRANSWICK, G. SIMPSON, H. E. STEARNS, AND P. VESTERGAARD, *Rockland State Hospital, Orangeburg, N.Y.*

MY–3033. **The Psychophysiology of Dreaming.**

The effects of tranquilizers on duration, frequency, and content of dreams are to be investigated in psychiatric patients. Dreams under drug conditions will be compared with those recorded in psychotherapeutic sessions when drugs are not given. EEG's, eye-movement recordings, and other physiological measurements will be made continuously during sleep. Differences between ability to remember and accurately relate dreams will also be noted for the drug and no-drug conditions.

Roy M. Whitman and Chester M. Pierce, *University of Cincinnati, Cincinnati, Ohio.*

MY–3050. **Metabolism of Biogenic Amines in Relation to Mental Illness.**

The metabolism and biosynthesis of biogenic amines (serotonin, catecholamines, neuraminic acid) will be investigated. The studies include the influence of vitamins, drugs, and physical therapy in patients. The effects of drugs on the amine content of animal tissue and body fluids of man will be measured, and correlations of results from animal tests with clinical data will be attempted. The levels of amines in body fluids in relation to clinical responsiveness to drug, insulin, and electroshock therapy will be studied in patients with mental and other clinical disorders.

Robert A. Cleghorn, *McGill University, Montreal, Canada.*

MY–3078. **Mast Cells of the Skin and Tranquilizer Therapy.**

The mast cells in skin specimens from normals and psychiatric patients will be compared. Skin biopsies from the psychiatric patients will be made again after six months' treatment with chlorpromazine to determine whether the drug has caused any mast-cell changes. An attempt will be made to determine the relationship between type of mental disturbance, outcome of treatment, and disturbances in mast cells.

Jacques LeBlanc and Lionel Lemieux, *Laval University, Quebec, Canada.*

MY–3226. **Imipramine Effects Before and After Norepinephrine.**

This is a controlled study of the effects of psychological, physiological, and metabolic responses to infused dihydroxyphenylalanine in a series of depressed patients who are on maintenance dosages of antidepressive drugs.

Dale G. Friend, *Peter Bent Brigham Hospital, Boston, Mass.*

MY–3253. **Hallucinatory Behavior of Normals and Schizophrenics.**

These investigators are attempting to determine whether normal subjects who hallucinate under the influence of LSD, hypnosis, or sensory isolation are able to experience visual hallucinations which are not artificially induced by these means, whether the "imagery" ability of nonhallucinating schizophrenics differs from that of schizophrenics who hallucinate, and whether there are physiological and psychophysiological correlates of visual or auditory hallucination.

Harry Freeman and Theodore X. Barber, *Worcester Foundation for Experimental Biology, Shrewsbury, Mass., and Medfield State Hospital, Harding, Mass.*

MY–3267. **The Psychophysiology of Dreams and Sleep.**

A number of investigations related to the utilization of supraliminal and subliminal stimuli in naturally occurring dreams and hallucinations and in dreams or hallucinations induced by LSD or hypnosis are to be carried out with normals, schizophrenics, alcoholics, and brain-damaged patients. Other aspects of these studies are concerned with the function of dreaming and with the effects of interruption or modification of the normal cyclic dream. Various drugs—e.g., chlorpromazine, reserpine, azacyclonol—will be used in an attempt to suppress dreaming.

Charles Fisher and William C. Dement, *Mount Sinai Hospital, New York, N.Y.*

MY–3308. **Relation of Behavioral Constellations to Drug Use.**

This investigation is designed to test hypotheses concerning the relation of changes in body image, body awareness, and self-concept to therapeutic reorganization and improvement of disturbed behavioral patterns, and to investigate the effects of drugs on such changes. Psychotic patients whose behavioral constellations are categorized as apathetic or extravagant will be treated with chlorpromazine, trifluoperazine, and thioridazine in rotation. Assessment procedures include galvanic skin response, motor tasks, body-sensing movements (touching, yawning, etc.), Rorschach tests, tests based on the Ames Illusions, Draw-a-Person Test, Twenty-Statements Problem, block design and object assembly, and ratings of ward behavior.

Robijn K. Hornstra and Thomas S. McPartland, *Greater Kansas City Mental Health Foundation, Kansas City, Mo.*

MY–3312. **The Effects of Centrally Acting Drugs on Behavior.**

The extent and nature of the behavioral effects of acute and chronic administration of barbiturates, alcohol, tranquilizers, and antidepressives are to be studied in animals (rats and mice), normal volunteers, schizophrenics, and other psychiatric patients. A large battery of psychological tests, including tests of psychomotor performance, perception, and intelligence, will be used. The

effect of experimental setting and motivation on drug response will be studied, as will inter- and intra-individual differences in response to drug. Operant conditioning procedures and maze-swimming tests will be used in the animal studies.

CONAN KORNETSKY, *Boston University, Boston, Mass.*

MY–3561. **Psychotropic Drugs and Autonomic Dysfunction.**

This is a long-term investigation of the interrelation between autonomic disturbance, psychological functioning, and drug effects in normal subjects and anxiety-neurotic patients. Drugs will be chosen according to their sites of action in the peripheral and central nervous systems. The effects of two laboratory stress situations (delayed auditory feedback and distraction during difficult mental activity) will be measured by muscle tension, pulse rate, pulse volume, finger volume, respiration rate, blood pressure (continuously recorded), motor coordination, level of aspiration, accuracy of judgment, judgment time and pattern discrimination, intellectual performance, emotional state (as determined by a check list of emotions), extraversion and neuroticism, mental state and symptoms as assessed by a questionnaire and by psychiatric interview. Autonomic responses will be used in quantitative pharmacological comparisons of the central and peripheral effects of the drugs. Drugs to be used initially are chlorpromazine, phenoxybenzamine, bretylium tosylate, and methacholine. Drugs with an atropinelike action, drugs which interfere with neuromuscular transmission, and possibly others will be used later.

HEINZ O. SCHILD AND MICHAEL SHEPHERD, *University College London, London, England.*

MY–3612. **Performance as a Function of Drive Level.**

This study is testing the hypothesis that an increase in drive level results in the use of fewer cues available in a given performance situation. Under varying conditions of drive, psychiatric patients and normal subjects will be presented with task relevant and irrelevant cues involving several dimensions (modality, number, intensity, sequence, rate, etc.) and complexity of response. An automatically programmed multi-cue display apparatus will be used. Drive conditions will be varied; different sets of instructions, psychiatric subjects differentiated as to drive level, and personality tests will be used. It is also planned to investigate the effects of drugs.

JOHN N. AGNEW, *University of Saskatchewan, Saskatoon, Saskatchewan, Canada.*

MY–3644. **Psychochemical Studies with Serotonin and Ammonia.**

This project consists of two separate studies. In one, psychiatric interviews and psychological tests will be used to evaluate the psychological and behavioral effects of alterations in brain serotonin levels in schizophrenics and schizophrenics in remission. Brain serotonin levels will be altered by administration of 5-hydroxytryptophan, and by 5-hydroxytryptophan combined with BAS, with reserpine, or with an MAO inhibitor. A double-blind methodology will be used. Chemical determinations of urinary excretion products and blood serotonin will be made for all subjects. The second study will test the hypothesis that prolonged hyperammoniemia causes characteristic changes in mental status and in the EEG. An attempt will be made to correlate the psychiatric and psychological effects with the EEG and biochemical effects of variations of blood ammonia levels in patients with liver disease.

GERALD D. KLEE AND SAMUEL P. BESSMAN, *University of Maryland, Baltimore, Md.*

MY–3663. **Psychopharmacological Studies of Adrenergic Transmitters.**

This broad interdisciplinary program of research will include investigations of the biosynthesis, distribution, interactions, release, and catabolism of adrenaline, noradrenaline, and related endogenous substances; pharmacological and physiological studies, in animals and in psychiatric patients, of the modes of action of sympathomimetic agents and their alteration by psychopharmacological agents; animal behavioral studies of the effects of alterations in the synthesis, storage, release, levels, transport, and catabolism of sympathomimetic amines in the CNS. Findings will be used as the basis of metabolic and psychological studies of psychiatric patients.

WILLIAM G. CLARK AND W. H. GRIFFITH, *University of California, Los Angeles, Calif.*

MY–3666. **Cerebral Metabolism of Neurohormonal Precursors.**

Cerebral blood flow determinations and $C^{14}$-labeled precursors will be used in in vivo studies of the decarboxylation reactions involved in the formation of serotonin, γ-aminobutyric acid, hydroxytyramine, and ethanolamine in the human brain. Following work with normal subjects, changes in these enzyme activities will be studied in mental disease and in psychiatric patients being treated with shock, drugs, or psychotherapy.

WILLIAM SACKS, *Rockland State Hospital, Orangeburg, N.Y.*

MY–3826. **Effects of Tranquilizers on Group Behavior.**

Indexes of total ward noise and patient movement are being developed and standardized for use in evaluating the effects of drug therapy on groups of patients as opposed to individual patients. Total ward noise is measured electronically, and a photoelectric grid is used to obtain measures of amount and speed of patient movement; nocturnal activity is measured by movement-

counters attached to the springs of the beds. These indexes are to be used in studies of the comparative effects of various tranquilizers in chronic psychiatric patients exhibiting noisy, disturbed behavior, and will be compared with clinical response and ratings on the Jenkins Symptom Rating Sheet, the Barrabee-Hyde Social Adjustment Scale, and the Gilbert and Wells Ward Socialization Index. Ratings and indexes will be made before, during, and after the medication period. Profiles of each drug's effects on groups of patients will be constructed.

ANTON F. HEUSLER AND GEORGE ULETT, *St. Louis State Hospital, St. Louis, Mo.*

MY–3929. **Metabolism of Chlorpromazine in Psychiatric Disorders.**

The structure and distribution of chlorpromazine metabolites excreted in urine and the relationship between chemical findings and the type of psychiatric disorder, patient response, and incidence of side effects are being studied in psychiatric patients. In vitro studies of the metabolism of chlorpromazine by human liver will also be carried out. The aim of the study is to delineate major chlorpromazine urinary metabolites in man and to correlate the therapeutic action of the drug with metabolic patterns.

VIVIAN FISHMAN, *Hillside Hospital, Glen Oaks, N.Y.*

MY–3951. **Central Nervous Control of Corticotropin Release.**

This is an investigation of the effects of various drugs, naturally occurring psychosis, and both spontaneous and induced anatomical lesions on the activation of pituitary corticotropin release, the response which mobilizes ACTH. ACTH secretion will be activated by use of an adrenocortical enzyme inhibitor, 1-2-bis-(3-pyridyl)-2-methyl-1-propanone (SU–4885), which blocks cortisol and acts as a stimulus to ACTH secretion. The secretion of ACTH can then be measured as 11-desoxycortisol in body fluids or by the urinary excretion of 17-ketogenic steroids. Testing will be done with drugs affecting the central nervous system, such as anesthetics, narcotics, sedatives, analeptics, psychotomimetics, phenothiazines, reserpine, meprobamate, and other psychopharmacological agents. Animal studies will be carried out with guinea pigs and dogs. Patients with anatomical neoplastic lesions, patients with anxiety reactions, depression, or schizophrenia, and normal subjects will also be studied.

PETER H. FORSHAM, *University of California Medical Center, San Francisco, Calif.*

MY–3967. **Chlorpromazine Metabolism in Psychotic Patients.**

This investigation will attempt to correlate clinical changes in psychotic patients with the metabolism of chlorpromazine in an effort to account for differing rates of regression in patients when the drug is withdrawn. The patients to be studied are male chronic schizophrenics. The metabolic studies will consist of determinations of the amount of free chlorpromazine and its sulfoxide being excreted in the urine. Paper chromatography will be used to determine whether there are qualitative metabolite differences in rapidly regressing patients vs. those regressing more slowly following discontinuation of drug. Clinical status of the patients will be quantitated by use of the Multidimensional Scale for Rating Psychiatric Patients.

ALBERT A. KURLAND AND CHIEN LI HUANG, *Spring Grove State Hospital, Baltimore, Md.*

MY–3968. **Phenothiazine Metabolism in Psychiatric Patients.**

The extent and nature of metabolic products of tranquilizing drugs of the phenothiazine type are being studied in neuropsychiatric patients by means of paper chromatography and a spectrophotometric procedure. Similarities and differences in metabolities resulting from different drugs of the phenothiazine class are also being investigated. $S^{35}$-labeled thioridazine will be administered to one catheterized patient to insure a complete quantitative 24-hour urine sample; determinations of the amount, distribution, and percentage of the metabolites in the urine sample will be made. The drugs being investigated are chlorpromazine, promazine, triflupromazine, prochlorperazine, trifluoperazine, perphenazine, thioridazine, and SC–10490.

SAMUEL EIDUSON AND NORMAN Q. BRILL, *University of California, Los Angeles, Calif.*

MY–4074A. **Effects of Epinephrine on Behavior.**

This project will attempt to correlate emotional state with concentration of adrenal hormones in the blood. It is a double-blind, own-placebo-control study of the effects of experimentally controlled variations in circulating blood levels of epinephrine on behavior, blood pressure, and pulse rate in hospitalized schizophrenic or depressed patients. The experimental procedure calls for uninterrupted infusion of physiological saline or one of the catechols for a period of several hours, during which time blood pressure and pulse rate will be continuously recorded, the subject will be interviewed hourly, mental status will be continuously evaluated, and the subject will be asked to report his sensations, thoughts, and fantasies. Prior to the experimental phase, all patients will be evaluated psychiatrically. Psychological tests and social service data will also be used in evaluations and diagnoses.

MARCUS A. JACOBSON AND GENE H. BOROWITZ, *University of Illinois, Chicago, Ill.*

MY–4137. **Pharmacologic Blocking of Alpha Chloralose Activation.**

Hospitalized psychiatric patients are to be used in this study, which will attempt to determine which drugs, if

any, block alpha chloralose activation of paroxysmal hypersynchronous EEG activity. The assumption, based on previous studies, is that such activation is indicative of CNS instability, which in turn is correlated with severe, episodic behavior disorders. Drugs assumed to inhibit this effect, such as nicotinic acid, ethoxyzolamides, and others not usually used in psychiatry, and proved antiepileptic drugs are to be used.

RUSSELL R. MONROE, *University of Maryland, Baltimore, Md.*

MY–4260. **Predictors of Drug Response in Schizophrenia.**

Through multivariate analysis procedures applied to a double-blind, placebo-controlled investigation, an effort will be made to delineate the psychological, biochemical, psychiatric, and behavioral variables which can best predict response to chlorpromazine in chronic schizophrenic women. Further, selected response measures are to be combined to give a general response index reflecting overall change. The stability of individual responsiveness on successive trials will also be studied. Measures of response to drug will be clinical improvement as evaluated by the psychiatrist, psychiatric aides' ratings of patients on the Oklahoma Behavior Scale (which covers communicativeness, activity, aggressiveness, sociability, grooming, and mood), ratings on the Psychologists' Rating Scale (which covers ideational fluency, cooperativeness, expressiveness and gestures, motor behavior, and mood), performance on the Purdue Peg Board and on Digit Symbols, and psychologists' ratings of the patients on the Clyde Mood Scale. The predictor variables to be investigated are history and background from the patients' records, particular categories of psychopathology, measures of autonomic function (galvanic skin response and oxyhemoglobin reduction time), projective tests (Drawing Completion Test and Word Association Test), biochemical variables (serum cholesterol levels and fasting blood glucose levels), red blood cell and plasma cholinesterase activity, and determinations of metanephrine, normetanephrine, and 3-methoxy-4-hydroxy-mandelic acid in urine.

MERVIN L. CLARK, CARL W. SMITH, AND THOMAS S. RAY, *University of Oklahoma, Oklahoma City, Okla.*

MY–4391. **Activity Level in Defectives and Normals.**

More precise methods of measuring total activity levels are being developed. The effects of tranquilizers, auditory, visual, and social stimulation, and other variables on activity level will be measured in mentally defective and normal subjects. The relation of subjective physiological variables to activity levels and to the effects of operant conditioning will also be investigated.

RUE L. CROMWELL AND JAMES G. FOSHEE, *George Peabody College, Nashville, Tenn.*

MY–4408A. **Study of GSR Response in Sedation Threshold Procedure.**

The diagnostic significance of sedation threshold is being investigated in schizophrenic patients, psychoneurotic depressed patients, and normal subjects. Galvanic skin reflex, basal resistance, EEG, and electromyograms will be used to measure levels of arousal, and the relation of arousal patterns to diagnosis and psychological test performance will be studied. The drug to be employed is thiopental sodium. Findings from this work will be compared with those which have been reported from similar studies by Shagass.

HARLEY C. SHANDS, *University of North Carolina, Chapel Hill, N.C.*

MY–4543. **Metabolism of Psychotropic Drugs.**

In a continuing study of the biochemical aspects of the action of psychopharmacological agents, variations in the responses of depressed and agitated patients to imipramine and chlorpromazine (which are structurally related but differ in metabolic patterns) will be investigated by studying urinary metabolite excretion patterns in vivo. The drugs will be administered simultaneously and singly and the results compared. Biochemical findings are to be correlated with the therapeutic response to assess dissimilar metabolism patterns for the two drugs in individual psychiatric patients.

VIVIAN FISHMAN, *Hillside Hospital, Glen Oaks, N.Y.*

MY–4567. **Biochemical Tests for Schizophrenia.**

A number of clinical and experimental tests are being used in research aimed at determining the direct and indirect influence of drug treatment and other psychiatric therapies on the results of biochemical tests. Of particular interest is the development of a method of preventing the effects of prior treatment from contaminating data being sought on a current treatment. Hospitalized patients on stabilized diets will be tested before, during, and at termination of drug therapy (chlorpromazine or iproniazid), ECT or other therapy.

ARTHUR YUWILER, *University of Michigan, Ann Arbor, Mich.*

MY–4579. **Visual Functions in the Schizophrenic.**

This study, which is part of a broader program of research on schizophrenia and drug action, is expected to provide information about the dynamic activity of the schizophrenic nervous system. Psychophysical methods will be used to study such aspects of visual and retinal functioning as spatial and temporal summation, hallucinatory activity, and neural effects of psychopharmacological agents in schizophrenic patients and normals.

LLOYD H. BECK, *University of Michigan, Ann Arbor, Mich.*

MY–4586. **Clinical-Metabolic Study of Depressive Illness.**

This is a double-blind, controlled investigation of the relation of norepinephrine to depression. DOPA (dihydroxyphenylalanine) or control saline will be given to chronic patients presenting depression as the major psychopathological symptom. Following administration of DOPA, which is a metabolic precursor of norepinephrine, patients will be placed on isocarboxazid (an MAO inhibitor and antidepressive) or imipramine (an antidepressive which does not inhibit MAO). Plasma catecholamine levels will be correlated with mood as measured by the Clyde Mood Scale, a direct mood questionnaire, and a brief psychiatric interview aimed at assessing mood.

DALE G. FRIEND, *Peter Bent Brigham Hospital, Boston, Mass.*, and JOHN E. SNELL AND MILTON GREENBLATT, *Massachusetts Mental Health Center, Boston, Mass.*

MY–4758. **Immediate Effect of Chlorpromazine on Verbal Behavior.**

The influence of chlorpromazine and placebo on verbal behavior in schizophrenics and normals will be investigated under conditions of reinforcement and extinction. The following aspects of verbal behavior will be studied: content, spontaneous output of affect statements during a controlled interview, differential output of affect under conditions of interviewer approval and subsequent absence of approval during a controlled interview and in a noninterview situation. Patients' ability to communicate under varying drug dosages will be evaluated. Drug effects on conditioned emotional response and bodily movements will also be investigated.

JOSEPH ZUBIN AND KURT SALZINGER, *New York State Department of Mental Hygiene, New York, N.Y.*

MY–4759. **The Effect of Chlorpromazine on the Pupillary Reflex.**

The effect of various dosage levels of chlorpromazine or placebo on pupillary reaction to sensory stimuli will be investigated in schizophrenics and normals to determine the adequacy of this method for studying the effects of chlorpromazine, to compare various types of schizophrenics with each other and with normals as to chlorpromazine's effect on pupillary reflex, and to compare pupillograms obtained under chlorpromazine with experimental manipulation of the pupillary reflex through ablation, sensory stimulation, and other techniques.

JOSEPH ZUBIN, GAD HAKEREM, AND SAMUEL SUTTON, *New York State Department of Mental Hygiene, New York, N.Y.*

## *Psychological and Physiological Studies with Normal Human Subjects*

MY–987. **The Effects of Certain Drugs on Personality.**

This is a long-term program of research on individual differences in drug responses and the relation of such differences to personality and body type. Double-blind studies of the effects of various types of drugs (e.g., morphine, heroin, papaverine, barbiturates, amphetamine, and alcohol) on mood, attitudes, motivational states, aggression, aggression-anxiety, self-concept, and other dimensions of personality and of the psychological mechanisms mediating drug-induced changes in mood and behavior will be carried out with normal subjects. Subjective and objective responses to drugs are to be compared with differences in personality and, if possible, with body type. The various assessment and screening measures include the Rorschach, Thematic Apperception Test, Edwards Personal Preference Schedule, observer-rating and self-rating scales, classification by the Sheldon somatotype system, the Wendt, Nowlis and Nowlis Adjective Checklist, a Picture Aggression test modeled after the Rosenzweig picture test, and a projective interview in which the subject elaborates on selected responses he has given in certain of the test situations.

HENRY K. BEECHER, *Massachusetts General Hospital, Boston, Mass.*

MY–2612. **Effects of Stimulant and Depressant Drugs.**

This investigation will test certain deductions from a general theory of the psychological effects of stimulant and depressant drugs. The theoretical postulate is that depressant drugs increase inhibitory potential, while stimulant drugs increase excitatory potential. The research is to be carried out with volunteer subjects. The first aspect of the study is concerned with drug effects on reminiscence and on massed vs. spaced practice effects in conditioning and learning tasks (eyeblink conditioning, pursuit-rotor learning, and the learning of nonsense syllables). The second phase of the study will test hypotheses concerning drug effects on visual figural aftereffects, auditory vigilance, and response to successive visual stimuli. Finally, canonical variate analysis, a data analysis technique new to psychological and psychiatric studies, will be used in the analysis of the drug effects obtained, and the possible uses and advantages of this method in formalizing the classification of drugs will be investigated.

HANS J. EYSENCK, *Maudsley Hospital, London, England.*

MY–2684. **Psychological Opposition of Reserpine and Iproniazid.**

The effects of reserpine, iproniazid, and placebo will be compared in controlled studies of normals (paid volunteers or prison inmates) to test hypotheses concerning mood and motivation and to develop and refine methods of assessing drug effects. Drug effects on mood, efficiency and motivation, and perceptual concomitants of mood will be assessed through adjective check lists, Q-sort techniques, and structured interviews; tests of cognitive performance, persistence under monotonous conditions, response tempo, and aspiration; measures of apparent size, time estimation, and perceptual distortion. An attempt will also be made to correlate pulse and blood pressure measurements, blood serotonin levels, and other physiological and biochemical observations with psychological findings.

CHESTER C. BENNETT, *Boston University, Boston, Mass.*

MY–2720. **The Effects of Alcohol as Related to Personality.**

A number of conditioning procedures and personality, psychomotor, and other behavioral tests are to be used to determine the similarity of the behavioral effects of alcohol to the behavioral effects of previously studied depressant drugs (amobarbital sodium and methylpentynol). The relation of personality to the effects of alcohol is also to be investigated, with emphasis on introversion-extraversion. The work is to be carried out with normal human subjects. Assessment procedures to be applied before alcohol intake are the Maudsley Personality Inventory, a questionnaire on drinking patterns and tolerance for alcohol, the Cattell 16 Personality Factor Questionnaire, and the Guilford-Zimmerman Scale. Procedures to be applied after the subjects receive alcohol or placebo include galvanic skin reflex, pursuit rotor, kinesthetic figural aftereffect, reaction time, Necker Cube, Archimedes Spiral, subtests of the Wechsler Adult Intelligence Scale, Porteus Mazes, mirror drawing, and determination of blood alcohol levels.

CYRIL M. FRANKS, *New Jersey Neuro-Psychiatric Institute, Princeton, N.J.*

MY–2726. **Experimental Human Psychopharmacology.**

A number of experimental studies of the effects of drugs and placebo and of the role of personality and other factors in modifying these effects will be carried out with normal college students. The drugs being studied include several phenothiazines, meprobamate, phenyltoloxamine, secobarbital, and others. A series of drug-action profiles—the characteristic patterns of a drug's action on physiological functions, psychomotor activity, psychological test and learning performance, interpersonal interaction, and psychodynamic processes—will be developed for various drugs at different dosage levels. Hypotheses relating to the role of personality in modifying drug action will be tested. An attempt will also be made to isolate and examine personality factors which may be related to reaction to placebo.

ALBERTO DIMASCIO, MILTON GREENBLATT, AND LESTON L. HAVENS, *Massachusetts Mental Health Center, Boston, Mass.*

MY–2922. **Effects of Drugs on Mood and Performance in Industry.**

The comparative effects of meprobamate, amobarbital, dextro-amphetamine, and placebo on work performance and mood (as measured by the Clyde Mood Scale) were investigated in a double-blind study using office workers as subjects. Preliminary data suggest differential effects of drugs on mood in workers classified as "stable" as opposed to those who are "mildly neurotic." The original study is now being repeated in additional groups of subjects. As in the initial study, the Clyde Mood Scale and a timed performance test will be applied before and after treatment.

LEON J. WARSHAW, *United Artists Corporation, New York, N.Y.*

MY–2971. **Psychological Responses to Changes in Blood Chemistry.**

Absolute and differential discriminative thresholds for various substances administered extra-orally are to be determined in normal human subjects. An apparatus is being developed which will permit controlled intravenous injection of chemical stimuli. Special attention will be given to subjective factors such as pain, hunger, and mood; suggestive factors in hunger and pain will also be studied. Since there is evidence that drugs administered extra-orally may produce distinctive sensory stimuli, this work is closely related to the problem of controls in drug-placebo evaluations.

HENRY K. BEECHER, *Massachusetts General Hospital, Boston, Mass.*

MY–2980. **Diagnostic Significance of Variations in Fantasy.**

The effects of tranquilizers, alcohol, caffeine, and various naturally occurring conditions on fantasied stories about pictures will be investigated. The fantasies are to be analyzed, coded, and correlated with the subjects' psychological state or diagnosis, and an attempt will be made to discover signs which have diagnostic significance.

DAVID C. MCCLELLAND, *Harvard University, Cambridge, Mass.*

MY–3032. **Behavioral Drug Effects in Animals and Man.**

Operant conditioning techniques will be employed in a systematic comparison of the behavioral effects of

psychoactive drugs in animal and human subjects.

FRANCIS MECHNER, SAMUEL IRWIN, AND F. M. OFFENKRANTZ, *Schering Corporation, Bloomfield, N.J.*

MY–3034. **Psychopharmacological Agents and Oculomotor Responses.**

The effects of barbiturates, tranquilizers, and psychotomimetics on eye movement and response patterns will be investigated in normal subjects presented with visual stimuli. The aims of this study are to develop tests of drug dosage, to increase understanding of sites and modes of drug action, and to localize more specifically the neural centers for eye movements.

GERALD WESTHEIMER, *Columbus Psychiatric Institute and Hospital, Columbus, Ohio.*

MY–3037. **Studies in Sensory Deprivation.**

Following psychiatric and psychological evaluations of the effects of sensory deprivation on volunteer, normal subjects, the effects of prochlorperazine, meprobamate, dextro-amphetamine, and placebo on behavioral changes induced by sensory deprivation will be studied. Assessment procedures include tests of personality, symptom check lists, psychomotor performance, tests of reasoning, and subjective reports of reactions.

JOHN C. POLLARD, *University of Michigan, Ann Arbor, Mich.*

MY–3167. **Experimental Analysis of Behavior Under Anesthesia.**

Free-operant behavior—in this case, manipulating a hand switch to eliminate or lessen an auditory stimulus—will be used as a measure of depth and duration of anesthesia in surgical patients. The effectiveness of this method of measuring depth of anesthesia will be compared with the effectiveness of EEG's and clinical observations. Thiopental sodium, cyclopropane, and ether are the three anesthetics to be used. The effects of operative trauma, hypoxia, and hypercarbia on free-operant recovery patterns are also to be investigated.

BENJAMIN ETSTEN, *New England Center Hospital, Boston, Mass.*

MY–3311. **Psychopharmacological Agents: Human Behavior Responses.**

A program of psychopharmacological research is being established which will investigate the effects of various psychopharmacological agents and possibly other drugs on human behavior. Types of behavior to be investigated include discrimination, perception, learning, and the effects of positive and negative reinforcers on performance. Normal human subjects will be used for most of the work.

AUDREY R. HOLLIDAY AND JAMES M. DILLE, *University of Washington, Seattle, Wash.*

MY–3313. **Psychopharmacology of Learning, Perception, and Skill.**

The effects of psychopharmacological agents on selected areas of behavior are being investigated in a long-term program of research. The interest is primarily in human behavior, but some of the work will be carried out with animal subjects. Specifically, the investigators will selectively modify processes of memory and learning, perception, and motor skills in order to analyze the contribution of each process to different kinds of behavior. The effects of various drugs on these behaviors will be compared in order to establish differential actions of drugs. Individual differences in susceptibility to drugs will be related to measures of behavior and personality. Among the drugs being used are depressants (including an anesthetic and a barbiturate) stimulants, and drugs reported to have specific effects on memory and on sensory and motor processes.

ARTHUR SUMMERFIELD, HANNAH STEINBERG, AND G. C. DREW, *University College London, London, England.*

MY–3375. **Effect of Drugs on Vocal Behavior.**

Measures of pattern of utterance durations, speech rate, speech volume, and changes in fundamental pitch will be used in this investigation of the behavioral effects of drugs (sedatives, stimulants, tranquilizers, antidepressives, and hallucinogens). Changes in vocal activity will be related to certain electrophysiological measures indicative of emotional response. Other measures include performance on a simple psychomotor task and scores on the Clyde Mood Scale. Normals in real-life and other situations will be studied, as will the effects of drugs on vocal behavior of outpatients in psychotherapy.

JOHN A. STARKWEATHER, *Langley Porter Neuropsychiatric Institute, San Francisco, Calif.*

MY–3616. **Development of Tests Sensitive to Drug Effects.**

There are essentially two phases of investigation in this project. The first is concerned with the development of objective tests of certain psychological and physiological functions such as psychomotor performance and visual and auditory perception. The investigators hope to increase the sensitivity of the tests by comparing various parameters of the tests and selecting the most sensitive ones. The second phase involves carefully controlled experimental studies of the effects of five dose levels of such drugs as caffeine citrate, dextro-amphetamine, secobarbital, meprobamate, chlorpromazine, and possibly others on the performance of normal subjects on the tests which have been developed.

J. RUTSCHMANN AND DONALD J. DILLON, *New York State Psychiatric Institute, New York, N.Y.*

MY–3966. **Effects on Memory of Induced Changes in Alertness.**

This study is testing in normal human subjects the hypothesis that level of alertness or degree of distraction intervening between acquisition and recall may contribute to the magnitude of forgetting which occurs between acquisition and recall. Following a period in which nonsense syllables and location of objects on a map are learned to criterion, levels of alertness will be altered by use of (*a*) drugs (pentobarbital sodium, methamphetamine, or saline), (*b*) performance tasks requiring and measuring differing degrees of alertness, (*c*) scheduled programs of activity, and combinations of these situations. Recall of the nonsense syllables and the location of objects on a map will be related to degree of alertness, distraction, or arousal during the period intervening between learning and recall.

GARDNER C. QUARTON AND GEORGE A. TALLAND, *Massachusetts General Hospital, Boston, Mass.*

MY–4681. **Effects of Drugs on Emotional and Motivational States.**

Research data in the general area of drugs and behavior are being prepared for publication. The data are from studies of drug effects on emotional and motivational states, motion sickness, vestibular function, and eye movements, as well as studies of the interaction of behavior systems at the reflex level, and adaptation and aftereffect in visual perception.

GEORGE RICHARD WENDT, *University of Rochester, Rochester, N.Y.*

MY–4742A. **Subjective Response to Intermittent Photic Stimulation.**

The relationship between individual subjective responses and EEG responses to photic stimulation and the effects of certain drugs on these responses are being studied in nonpsychotic, non-brain-damaged subjects. Individual consistency of response within and between test sessions and changes in responses occurring during the drug and no-drug periods are being investigated. Subjective responses will be recorded in the following categories: visual and nonvisual sensations, general emotional and abstract reactions, organized hallucinations, clinical pathological states, and seizures. An attempt to correlate Rorschach responses with responses to photic stimulation will also be made. The drugs to be used are dextro-amphetamine, LSD, 1-ethyl-3-piperidyl benzilate HCl (JB–318), secobarbital, and chlorpromazine.

MARTIN H. KEELER, *University of North Carolina, Chapel Hill, N.C.*

## *Studies of the Effects of Drugs on Animal Behavior*

MY–487. **Investigation of Variables Affecting Avoidance Behavior.**

This project, part of a continuing investigation of the social, perceptual, and physiological aspects of emotional behavior, will investigate the communication of affects in man and monkeys by means of conditioned and autonomic responses; perceptual thresholds in normal and psychotic subjects by means of tachistoscopic techniques; and sleep patterns in monkeys by means of the EEG. A newly devised technique for studying communication of affect—requiring that one animal provided with the response mechanism perceive and respond to the behavioral cues of a second animal which is provided with the conditioned stimulus—will be used. Studies of frustration and of the role of pharmacological agents in the communicative process will make use of this new method. An attempt will also be made to determine the role of certain biochemical agents (physiologically active peptides, plasminogen activators, and neurohumors in blood and urine) in fear and anxiety. The techniques developed with animals will be extended and applied to studies in man.

I. ARTHUR MIRSKY AND ROBERT E. MILLER, *University of Pittsburgh, Pittsburgh, Pa.*

MY–647. **Behavioral Laws of Motivation and Conflict.**

This is a long-range program of basic research on motivation, reinforcement, and conflict. Behavioral, physiological, and pharmacological techniques are being used, and the effects of various kinds of drugs on behavior will be investigated in animals. Three drives—hunger, thirst, and fear—are of special interest.

NEAL E. MILLER, *Yale University, New Haven, Conn.*

MY–776. **Experimental Analysis of Imprinting.**

This is a broad program of research on the phenomenon of imprinting, an early and rapid form of learning. The effects of brain lesions, drugs, the stimulus factors prompting imprinting, the duration of imprinting, the effects of lack of imprinting on future behavior, and other aspects of imprinting are being studied in birds (water fowl), chicks, and guinea pigs.

ECKHARD H. HESS, *University of Chicago, Chicago, Ill.*

MY–928. **Response Variables in Classical Conditioning.**

This is a long-term investigation of neurophysiological variables in learning. An attempt is being made to develop standardized procedures for obtaining base lines

against which to evaluate and interpret physiological variables, including the effects of drugs and neurosurgery, and to develop a mathematical model for classical conditioning. The experimental subjects are dogs.

DONALD W. LAUER, *Indiana University, Bloomington, Ind.*

MY–1061. **The Modification of Fixated and Convulsive Behavior.**

Behavior rigidity in animals will be studied in an attempt to specify the psychophysiological events that lead to formation and maintenance of such rigidity. Also investigated will be the possibility that tranquilizing drugs may prevent or suppress behavior rigidity and that psychophysiological methods of drug assay involving learning, perception, and anxiety reduction can be developed. Rats will be used as subjects. Implanted electrodes, EEG's, soluble and insoluble problems, and induced seizures are among the techniques being employed.

ROBERT S. FELDMAN, *University of Massachusetts, Amherst, Mass.*

MY–1225. **Behavioral Effects of Drugs in Macaca Mulatta.**

The effects of depressant, stimulant, and psychotomimetic drugs on the following forms of learned or unlearned behavior in monkeys are being investigated: general activity, emotional reactivity, visual discrimination, and delayed response. Operant and classical conditioning techniques are employed. Behavioral profiles will be used for characterizing the drugs. Pentobarbital, chlorpromazine, mescaline, LSD, amphetamine, and caffeine are among the drugs being studied.

MURRAY E. JARVIK, *Albert Einstein College of Medicine, New York, N.Y.*

MY–1604. **Experimental Studies in Comparative Psychopharmacology.**

This is a broad program for the experimental analysis of drug-behavior interactions at various phylogenetic levels, the development of methods for preclinical screening and assessment of psychotherapeutic drugs, and the establishment of training facilities in psychopharmacology.

JOSEPH V. BRADY, *University of Maryland, College Park, Md.*

MY–1775. **Effects of Drugs on Psychological Development.**

A series of studies of the development of behavior patterns in dogs is being continued. On the basis of previous findings which indicate that complete isolation in early life introduces behavioral alterations that persist in adult life, and that limited social contact during the period of isolation prevents such alterations from being permanent, the investigators are now attempting to determine how much social exposure is necessary to preserve normality, and to determine the effects of pharmacological agents applied during the social exposure on subsequent behavior. Other aspects of the work involve studies of conditioning of puppies early in life, chronic stress during isolation, and drug effects on stimulus control of behavior, conflict, and consolidation of memory traces in mice. Operant techniques are to be used; schedules evaluating social motivation, discrimination learning, and emotional activity will also be applied.

JOHN L. FULLER AND LINCOLN D. CLARK, *Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine.*

MY–2094. **Basic Types of Effects of Drugs on Behavior.**

This long-term program of research is concerned with interactions between drug effects and behavior in animals and in man. Operant techniques are being used in controlled environmental situations. Of special interest are species differences and the significance of the particular motivations and the particular motor responses involved in the behavior affected by drugs. The effects of morphine, methamphetamine, amobarbital, chlorpromazine, l-epinephrine and related compounds on operant behavior under various conditions are being investigated in cats, monkeys, drug-addicted monkeys, fish, pigeons, mice, rats, dogs, chimpanzees, and man. The investigators hope to extend the work to studies of invertebrates and will attempt to develop sustained behavior in the octopus which would be suitable for investigations of drug effects.

PETER B. DEWS AND WILLIAM H. MORSE, *Harvard Medical School, Boston, Mass.*

MY–2273. **Effects of Drugs on Conditioned Emotional Responses.**

The effects of a number of treatments—including drug therapy, carbon dioxide, extremes of temperature, and various hormones—on conditioned fear and avoidance are being studied in laboratory animals. The investigator will test the hypothesis that the autonomic, endocrine, and extrapyramidal changes which occur during the learning of a conditioned emotional response acquire the properties of conditioning stimuli with respect to that response, and that any change in these aspects of the internal environment, as provoked by one of the treatments, will interfere with retention and extinction of the conditioned emotional response.

GORDON T. HEISTAD, *University of Minnesota, Minneapolis, Minn.*

MY–2312. **The Role of Nonaversive Conflicts in Behavior.**

This study is designed to test the relation between neurosis and conflictual approach-approach situations. Following a general adaptation to environment period,

alterations in adaptive patterns will be studied during and after the induction of experimental neuroses. Also, the modification of behavior by drugs will be studied in animals with and without brain lesions. Cats and primates are being used.

JULES H. MASSERMAN, *Northwestern University, Chicago, Ill.*

MY–2456. **Differential Extinction and Stimulus Control.**

This is a continuation of a long-term investigation of the role of stimuli in the control of operant behavior. The assumption that a single "excitation" process governs both acquisition and extinction is to be tested by comparing gradients of generalization of "excitation" with generalization of extinction functions, by determining whether the effects of reinforcement and those of extinction show the same pattern through time, and by determining the effects of phenobarbital on the modification of reinforcement and extinction processes.

DONALD S. BLOUGH, *Brown University, Providence, R.I.*

MY–2554. **Instrumental Generalization Gradients.**

Research investigating stimulus factors related to the generalization of response in operant behavior in rats is being continued. The form of the generalization gradient following discrimination training with different pairs of tones differing in loudness, and the effects of varying amounts of discrimination training are being studied. This work has implications for psychopharmacological studies employing operant techniques.

ROSEMARY PIERREL AND J. GILMOUR SHERMAN, *Barnard College, New York, N.Y.*

MY–2645. **Behavioral Effects of Phenothiazine Derivatives.**

This study is an extension of previous research on the use of operant conditioning methods to investigate the effects of drugs on learning in pigeons under varying reward conditions. Phenothiazine derivatives and other drugs are being systematically compared.

PETER B. DEWS, *Harvard Medical School, Boston, Mass.*

MY–2741. **Conditioning under Curarelike Drugs.**

The underlying aims of this research are to shed further light on various problems relevant to theories of learning, psychophysiology, and psychosomatic medicine. Specifically, studies of persistent conditioned emotional responses in curarized dogs, and the effects of such responses on the subsequent behavior of the same animals in noncurarized states are being conducted. Of particular interest are the refinement and development of conditioning techniques which will insure the emergence of the conditioned autonomic effects in the same subjects at a subsequent noncurarized period. Parametric analyses of the conditioned suppression technique are being made, a training procedure for conditioned suppression is being developed for use in analyzing the effects of sensory input and emotional conditioning under curarization on later behavior in the noncurarized state, and a training procedure for conditioned suppression is being developed for use in screening various curarelike drugs for dissociative effects.

ABRAHAM H. BLACK, *McMaster University, Hamilton, Ontario, Canada.*

MY–2814. **Screening CNS Drugs.**

A critical analysis will be made of the objective physiological signs and characteristic behavior patterns produced by several classes of centrally acting drugs in the rhesus monkey. The basic aims of the work are to develop a rapid method of screening drugs for potential therapeutic value, and to determine whether the overt effects of the different classes of drugs can be correlated with changes in brain function. Among the measures used are blood pressure, EKG, body temperature, respiratory rate, gross neurological effects, pupil size, piloerection, wakefulness, apprehension, defecation, and spontaneous EEG's.

GERALD A. DENEAU, *University of Michigan, Ann Arbor, Mich.*

MY–2839. **Pharmacology of Motivational Mechanisms.**

This study is aimed at developing drug screening techniques which will predict the motivational effects of drugs in man. The effects of a number of pharmacological agents, including tranquilizers, energizers, psychotomimetics, and "autonomic transmitters," on self-stimulation and avoidance behavior are to be investigated in rats and monkeys. Approach or avoidance behavior is to be induced by direct electrical or pharmacological stimulation of the parasympathetic and sympathetic regions of the brain.

JAMES OLDS, *University of Michigan, Ann Arbor, Mich.*

MY–2926. **Sensory and Motor Factors in Escape Conditioning.**

This is an investigation of the locus and mechanism of effects and side effects of morphine and chlorpromazine. Rats will be used in a number of conditioning experiments designed to measure interference with adaptive learning and performance.

HAROLD W. COPPOCK AND ROBERT A. PATTERSON, *Arizona State University, Tempe, Ariz.*

MY–2929. **Chlorpromazine Action on Amygdaloid-Septal Areas.**

The site of action of chlorpromazine, and possibly other drugs, is being investigated in studies of the effects of total or partial destruction of amygdaloid and septal areas on the ability of rats to adapt to stress (swimming). Normal and surgically prepared animals with and without drug treatment will be compared. The physiological activity of, and the interrelation between, the amygdaloid and septal areas are also being investigated.

JOHN W. NELSON AND ARTHUR TYE, *Ohio State University, Columbus, Ohio.*

MY–2949. **Analysis of Drug Effects on Fear and Conflicts.**

The aim of this long-term program of research is to develop new techniques for investigating and measuring the effects of fear and drug effects on fear in animals (rats and monkeys in particular). A wide variety of compounds (e.g., morphine, ethyl alcohol, chlorpromazine, amobarbital sodium, cocaine, methamphetamine, caffeine, and perphenazine) will be employed in avoidance conditioning and conflict producing experiments. The effects of drugs on chronic vs. acute stress and on drives aroused by conflict as opposed to drives aroused by fear will be studied by both newly developed and already existing techniques. The best measurement techniques and most effective drugs used in the work on technique development will be employed to compare drug effects in rats and monkeys.

NEAL E. MILLER AND HERBERT BARRY III, *Yale University, New Haven, Conn.*

MY–3017. **Drug Effects on Higher Adaptive Behavior.**

The effects of psychoactive drugs on complex behavior in animals are being investigated. Drug effects on social behavior, symbolic processes, and other higher adaptive behavior in rats, cats, or dogs will be investigated. Part of the work is devoted to the development or standardization of techniques and methods for comparative studies of higher adaptive behavior in several animal species.

LOH SENG TSAI, *Tulane University, New Orleans, La.*

MY–3029. **Evaluation and Pharmacology of Psychotropic Agents.**

The effects of various new drugs on general activity, locomotor activity, avoidance, and conditioned anxiety will be investigated in rats and mice and compared with the effects of known drugs. A second aspect of this work is concerned with the development of new techniques for screening drugs, including studies of the effects of known and new experimental compounds on stress-induced behavior in rats and the development of methods for determining the central autonomic and cortical effects of drugs. Behavioral and pharmacological studies of the effects of chronic administration of monoamine oxidase inhibitors will be investigated in rats, dogs, and cats, and the effects of antagonists of MAO inhibitors will be investigated in rats, dogs, and monkeys.

JOSEPH P. BUCKLEY AND WILLIAM J. KINNARD, JR., *University of Pittsburgh, Pittsburgh, Pa.*

MY–3229. **Effects of Psychopharmacologic Agents on Behavior.**

Studies of the acute and long-term effects of drugs on (*a*) behavior controlled by aversive stimuli, (*b*) conflict behavior, and (*c*) avoidance extinction are being carried out with dogs and monkeys.

BERNARD WEISS AND VICTOR G. LATIES, *Johns Hopkins University, Baltimore, Md.*

MY–3235. **Physiological Action of Psychopharmacological Agents.**

The effects of varying concentrations of LSD, bufotenine, yohimbine, meprobamate, and other psychopharmacological agents on behavior, particularly certain types of learned behavior, longevity, and the development of various organs are being investigated in lower vertebrates and invertebrates with simple central nervous systems. Among the experimental animals are earthworms, chameleons, mice, and several species of fish. Behavioral effects will be correlated with physiological and chemical (including histochemical and microchemical) findings in an attempt to learn more about the sites and mechanisms of action of the drugs studied.

CHARLES G. WILBER AND JOSEPH A. BURKE, *Loyola College, Baltimore, Md.*

MY–3238. **Interaction of Habit Strength and Drug Effects.**

Drug effects will be investigated in rats trained to various levels of performance, including different degrees of overtraining, to determine the interaction of habit strength and drug effects. Different types of drugs, different dosages, various levels of habit strength, various types of responses in positive and negative conditioning studies, motor control, muscular coordination, and general activity will be studied.

DALBIR BINDRA, *McGill University, Montreal, Canada.*

MY–3361. **Basic Mechanisms of Drug Action on Animal Behavior.**

This is a broad program of basic research on the effects of psychopharmacological agents and other compounds on animal behavior. Specific studies deal with the interaction of drug effects and brain lesions on emotional and abnormal behavior in animals, and with the genetics of CNS function and behavior. The emphasis of the research is on developing techniques for use in behavioral

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pharmacology and on investigating basic mechanism of drug action.

HOWARD F. HUNT AND BENSON E. GINSBURG, *University of Chicago, Chicago, Ill.*

MY–3364. **Neuropharmacological Studies of Motivational States.**

Several investigations of the effects of chemical or electrical stimulation of thalamic, hypothalamic, and limbic structures on motivational levels are to be carried out with rats. Implanted electrodes will be used for electrical stimulation; chemical stimulation will be accomplished via direct injection of chemical agents into various parts of the brain. Consummatory behavior, performance of a habit established by food reinforcement, and avoidance learning are the behavioral responses to be studied. An attempt will be made to relate motivational states and drug-induced changes in motivational states to drug effects on neurohumoral mechanisms.

NILS JAMES CARLSON AND T. GEORGE BIDDER, *Western Reserve University, Cleveland, Ohio.*

MY–3382. **Drug Effect on Positively Reinforced Operant Behavior.**

Several positive reinforcement schedules are being used to investigate the behavioral effects of various dose levels of chlorpromazine and amphetamine in pigeons. One phase of the study is concerned with the relation of drug dosage and past training history to changes in the effect of a conditioned (secondary) reinforcer.

DONALD C. MOSER, *Dickinson College, Carlisle, Pa.*

MY–3541. **The Effect of Selected Drugs on Learning.**

The effects of strychnine sulfate, sodium pentobarbital, and other neurochemical stimulants and depressants on learning in rats are being assessed. In some of the studies, the effects of drugs known to affect the acetylcholine-cholinesterase system will be evaluated in two strains of rats (Tryon maze-bright and Tryon maze-dull) which differ in brain cholinesterase activity and in learning ability. Other variables to be studied are dosage levels of the drugs, types of learning tasks, and time of injection of drugs.

JAMES L. MCGAUGH AND CALVIN W. THOMSON, *San Jose State College, San Jose, Calif.*

MY–3648. **A Screening Test for Tranquilizing Compounds.**

This is an evaluation of the use of operant techniques with rats as a method for screening psychopharmacological agents. Frequency of bar-pressing behavior in response to two alternating operant routines will be used as the criterion for comparing the effects of various drugs. In preliminary evaluations of the technique, the effects of known tranquilizers (e.g., chlorpromazine, promazine, meprobamate) will be compared with the effects of control compounds such as pentobarbital or phenobarbital. Other compounds which may be studied are methamphetamine and an analgesic.

JAMES A. DINSMOOR, *Indiana University, Bloomington, Ind.*

MY–3673. **Effects of Psychotropic Drugs on Sensory Processes.**

Operant conditioning techniques are being used in this investigation of the effects of drugs such as pentobarbital, amphetamine, and chlorpromazine on visual and auditory processes in pigeons. The work is oriented toward the development of techniques for screening drugs rather than toward the analysis of particular drugs. Techniques for measuring psychophysical functions in different animal species are also being developed.

FRED S. KELLER AND ROBERT BERRYMAN, *Columbia University, New York, N.Y.*

MY–3709A. **Effect of Methylphenidate on Stress and Learning.**

The effect of methylphenidate on discrimination and learning by rats in a Lashley jumping apparatus is being studied. The study is testing hypotheses related to the possible cortical-stimulating effects and the possible stress-reducing effects of the drug.

GEORGE J. LYTTON AND J. O. SINES, *Sheltering Arms Guidance Center, St. Joseph, Mo.*

MY–3801A. **Studies in Social Behavior and Escape and Avoidance.**

Two monographs are being prepared for publication. One, on social behavior in rats, will present findings on individual and paired interactional problem solving. The second one, reporting research on the long-range effects of severe trauma in weanling and adult rats on learning under stress, includes studies of the effects of age at time of trauma, the particular learning task involved, and drugs.

RICHARD A. LITTMAN, *University of Oregon, Eugene, Oreg.*

MY–3963. **Social Behavior in Psychopharmacological Screening.**

The effects of drugs—a tranquilizer, a barbiturate, and an antidepressive—on social interaction are being investigated in rats and mice housed in a quasi-natural environment in which food is accessible to only one animal at a time. Three groups of animals are to be used: one in which all animals are given drug, one in which all animals are given placebo, and one in which half are given drug and half placebo. Of particular interest are the establishment of, and drug-induced changes in, domi-

nance-submission hierarchies, the effects of the presence of female rats on such hierarchies, and the differentiation of effects of the three types of drugs. Preliminary studies with methylphenidate have shown not only that greater behavioral changes occurred in animals given drug than in animals given placebo, but that changes which occurred in the drug-treated animals affected their social interaction and thus indirectly affected the control animals.

RICHARD P. RUNYON AND WILLIAM J. TURNER, *C. W. Post College, Long Island University, Greenvale, N.Y.*

MY–3997. **Immediate and Delayed Effect of Severe Trauma.**

The long-term effects of trauma on subsequent behavior are being investigated in white rats subjected to severe but nonconvulsive electric shock at various ages—preweanling, weanling, adult, senescent. Parameters of the shock experience, residual effects of trauma on problem-solving and discrimination activities, involving various motivational conditions, the role of drugs in blocking the effects of trauma, and the effects of CNS lesions will be systematically studied.

RICHARD A. LITTMAN AND ROBERT W. LEARY, *University of Oregon, Eugene, Oreg.*

MY–4004A. **Quantitative Study of Visual Exploratory Behavior.**

The effect of successive light stimuli, presented singly or in pairs, on the bar-pressing response is being studied in rats. The aim of this study is to obtain a quantified function of the relationship between response strength and properties of stimulus consequences. The informational content of the stimulus configuration will be varied by altering the number of times the animal is permitted to respond. Following acquisition, the effects of cortical lesions on bar-pressing functions in retention and relearning will be investigated in an effort to delineate brain structures involved in visual reinforcement and exploratory behavior. The data obtained will provide a base line for future assessment of "activating" and tranquilizing drugs.

JOHN W. DONAHOE, *University of Kentucky, Lexington, Ky.*

MY–4038. **Factors Affecting the Alcohol Consummatory Response in Rats.**

This study is basically concerned with exploring etiological factors in alcoholism, particularly the interactive effects of genetic predisposition to alcohol consumption and certain learning experiences early or later in life. Following separation of groups of Wistar rats into high and low consumers during free alcohol-consumption periods, the effects on alcohol consumption of stress or other learning experiences (e.g., oral deprivation, auditory stimulation) which end or are anticipated simultaneously with the presentation of alcohol will be investigated experimentally. The relation of time of occurrence (i.e., early or later in life) of the stress or learning experiences will also be studied.

MAURICE KORMAN AND IRWIN J. KNOPF, *University of Texas, Southwestern Medical School, Dallas, Tex.*

MY–4056. **Autonomic Conditioning: Cardiac and Pupillary Studies.**

This research is attempting to determine whether the pupillary reflex to light can be conditioned in cats and rabbits. The use of food reinforcers and the effects of the training conditions on cardiac and respiratory activity will be investigated. The unconditioned stimuli to be used are onset and offset of light, and intracranial or peripheral shock. Operant and autonomic conditioning are to be compared, and the effects of tranquilizers on both types will be studied.

CELESTE F. MCCOLLOUGH, *Oberlin College, Oberlin, Ohio.*

MY–4139. **Drug Effects on Nondiscriminated Avoidance Behavior.**

The effects of drugs on nondiscriminated avoidance behavior (Sidman-type schedule) in rats are to be systematically studied and compared with drug effects on differential reinforcement for low rates of responding. In addition to conditioned behavior, spontaneous running activity, adaptation to novel situations, emotionality, and timidity will be measured. Dose-response curves will be determined for pentobarbital, chlorpromazine, amphetamine, benactyzine, scopolamine, atropine, and eserine. Later in the research, interactions of these drugs will be studied, and the effects of other drugs such as LSD, mescaline, or marijuana may be investigated. Interaction of drug effects with changes in shock intensity, duration of shock, and state of deprivation will also be explored.

GEORGE C. STONE, *Langley Porter Neuropsychiatric Institute, San Francisco, Calif.*

MY–4230. **Effects of Tetrahydrocannabinols on Animal Behavior.**

The behavioral effects of various tetrahydrocannabinol derivatives—related to the active principles of marijuana—are to be compared with the effects of pentobarbital, chlorpromazine, dextro-amphetamine, and reserpine. Drug effects on rats in various experimental situations will be examined. Specific types of behavior to be studied are operant behavior for food reward and for positively reinforcing intracranial self-stimulation, conditioned emotional response, and conditioned avoidance.

EUGENE S. BOYD, *University of Rochester, Rochester, N.Y.*

MY–4511. **Effects of Psychotropic Drugs on Experimental Stress.**

This is a controlled study of the effects of stress on the behavior of rats and of the effects of drugs on response to anxiety-producing situations. Stress conditions, which can be applied singly or in combinations, are to be flashing bright lights, oscillation, and audiogenic stimulation. The effectiveness of various drugs (including tranquilizers, barbiturates, stimulants, and antidepressives) in protecting the animals against the severe effects of anxiety will be evaluated by ability of the drugs to prevent the lethal effects of stress, drug effect on blood pressure, and drug effect on conditioned avoidance response. Drug effects on the alleviation of anxiety (as contrasted with the effects of anxiety) will be investigated in rats trained to a simple conditioned emotional response.

JOSEPH P. BUCKLEY AND MARIO D. ACETO, *University of Pittsburgh, Pittsburgh, Pa.*

MY–4705. **Effect of Anxiety and Stress on Simple Performance.**

This investigation is concerned with the interaction between manifest anxiety and experimentally induced variations in drive level on performance and generalization in simple, noncompetitive response situations. Several experiments designed to develop and evaluate theoretical reformulations of the summative interaction between induced anxiety and manifest anxiety, as these variables contribute to total drive, will be carried out. The effects of meprobamate and chlorpromazine on performance will be analyzed with a view to determining drug effects on temporal generalization gradients. The study will use rats in standard operant conditioning situations.

OTELLO DESIDERATO, *Connecticut College, New London, Conn.*

MY–4776A. **Exposure and Subsequent Sensitivity to Lysergic Acid.**

Siamese fighting fish (*Betta splendens*) are being used to study the effects of early exposure to lysergic acid diethylamide upon subsequent sensitivity to this drug at maturity. The effects of LSD on groups of mature fish which were exposed to either of two concentrations of LSD at the egg stage, as two-day-old fry, or as 10-day-old fry will be compared with the effects on mature fish which have had no previous exposure to LSD. The measures to be used are backward movement, head up at surface, Cartesian diver, barrel roll, body kinking, quiescence, slow movements, lateral displays, and darkened pigment.

JACK ARBIT AND BENJAMIN BOSHES, *Northwestern University, Evanston, Ill.*

MY–4789. **Multidimensional Behavioral Analysis of Drugs.**

One of the major aims of this work is to develop a methodology which will combine "naturalistic observation" with the experimental control and manipulation of variables for use in investigating learned and unlearned behavior in animals, determining the effects of chronic drug administration, and evaluating the usefulness of this technique as a means of screening psychoactive drugs. This work is to be carried out with rats, but the method can be modified for studies of other animals.

LEON S. OTIS, *Stanford Research Institute, Palo Alto, Calif.*

## *Studies of the Effects of Psychotomimetic Drugs*

MY–2251. **Ego Impairment with LSD–25 and Schizophrenia.**

This research, which is to be continued over a period of several years, will investigate the effects of LSD on ego function in normal subjects and compare the findings with the results from studies of ego function in schizophrenic patients. Throughout the work, emphasis will be on perception and communication. Specific techniques to be used include measures of size constancy, threshold of visual perception, autokinetic reaction time, time orientation, space orientation, systematic variations in interpersonal factors in the experimental situation (accomplished by manipulating experimenter attitudes), the use of free and zero feedback in certain kinds of communication, and analyses of form, content, and intonation of language. Longitudinal studies of the way in which subjects deal with drug experiences (with LSD and other compounds) will also be carried out.

WILLIAM E. MOONEY, *University of Pittsburgh, Pittsburgh, Pa.*

MY–2262. **Behavioral Effects of Lysergic Acid Diethylamide (LSD–25).**

This investigation of the behavioral effects of drugs, especially LSD, in normal and schizophrenic subjects is being carried out within the framework of the Werner-Wapner comparative-developmental theory. Hypotheses in the study are related to questions of whether changes induced by LSD are "developmentally regressive," that is, whether normal adults under LSD show behavior analogous to that of children and schizophrenic patients, and whether LSD in schizophrenics causes further regression than that which is already present. Drug effects on different areas of functioning which can be ordered according to time of appearance (i.e., early or late in the course of development) will be studied.

Among the tests of sensorimotor, perceptual, and conceptual processes which are being used are: static and dynamic body equilibrium as measured by an ataxiameter and stabilometer, a modified embedded figures test, rod-and-frame situation, tachistoscopic studies of emergence of figure from ground, sensitivity and apparent size of body parts (body image), problem solving, planning time alloted to part-activities of a complex whole, steadiness, apparent horizon, Stroop Color Words tests, and perhaps polygraph recordings of changes in muscular tension.

DONALD M. KRUS AND SEYMOUR WAPNER, *Clark University, Worcester, Mass.*

MY–2302. **Studies with New Hallucinogens.**

Comparative studies of the effects of LSD and JB–318 (1-ethyl-3-piperidyl benzilate hydrochloride) are being carried out with normal human subjects. Changes in mood, feeling, imagery, vigilance levels and attention, body image, and in general individual patterns of response to drugs are being assessed by an abbreviated form of the Thematic Apperception Test, psychiatric interview, the Rorschach test, the Behn-Rorschach, the rod-and-frame test, the Stroop test, the tilting-rod-tilting-chair test, estimation of apparent horizon, and the Clyde Mood Scale.

ADRIAN M. OSTFELD, *University of Illinois, Chicago, Ill.*

MY–2621. **Use of Psychotomimetics in Personality Evaluation.**

The effects of psychotomimetics (especially LSD) on individual characteristic defense mechanisms, ways of relating to others, ways of conceptualizing oneself, one's life goals, and one's difficulties are being investigated in psychiatric outpatients who are being evaluated for psychotherapy. Techniques include psychiatric observation, interviews, objective psychological tests, rating scales, role-playing, subjects' drug-state reactions to tape-recorded statements which they have made during their normal state. The emphasis of the study is on the relation of drug-state processes to ordinary waking-state processes and its significance to personality evaluation, diagnosis, and prognosis.

DON D. JACKSON, *Palo Alto Medical Research Foundation, Palo Alto, Calif.*

MY–3670. **Primary Process Thinking in Effects of LSD–25.**

A double-blind, controlled study of the effects of LSD on normals will be carried out to identify individual differences in reactions to the drug and to isolate personality variables that may predict the reactions of specific subjects. A cross-validational study of personality variables and the reactions to drugs will then be conducted with additional subjects. Comprehensive personality assessments will be made, and a battery of cognitive and emotional measures will be given before, during, and after drug. A secondary aspect of the study is concerned with the interrelations of different approaches to primary process thinking—reactions to LSD, perceptual isolation, projective tests, subliminal stimuli, and dreams.

ROBERT R. HOLT AND GEORGE S. KLEIN, *New York University, New York, N.Y.*

MY–4659A. **Prediction of Behavioral Changes Under LSD–25.**

This study will attempt to predict drug response on the basis of pre-drug measurements of personality variables. Behavioral changes in paid volunteer subjects under the influence of LSD are to be predicted from base-line reactions to an initial stress situation (delayed auditory feedback). Using a concept advanced by Funkenstein et al., the investigators will study two symptomatic groups: subjects showing anger-out (norepinephrinelike) response and those showing anger-in (epinephrinelike) response to initial stress situations. Measurements of autonomic functioning, psychiatric interviews, and the MMPI will be used prior to drug and during the period of drug effects. Behavior during drug will be observed and rated. The hypothesis is that the anger-out group will show a paranoid reaction to LSD whereas the anger-in group will show a depressive reaction.

MORRIS A. LIPTON, *University of North Carolina, Chapel Hill, N.C.*

## *Studies of Brain Mechanisms and Behavior*

MY–675. **Neurological Bases of Behavior.**

This is a long-term project investigating the neurological bases of behavior. Included in the study is an analysis of the effects of tranquilizing drugs upon experimentally induced behavior changes, upon learned performance, and upon induced seizures and associated electrographic phenomena. The experimental animals will be mainly cats and rats. Techniques and methods include the use of implanted electrodes, brain lesions, approach and avoidance conditioning, EEG, and neuroanatomic studies of brain tissue. Chlorpromazine, reserpine, and Tremorine are among the drugs employed.

WALTER R. INGRAM AND J. R. KNOTT, *State University of Iowa, Iowa City, Iowa.*

MY–993. **Slow Potential Changes in Conditioning.**

Brain recordings of conditioned animals, with special emphasis on slow electrical changes lasting for many seconds, are being studied. The animals are cats and monkeys, and both classical and operant conditioning are used. It is planned to use bio-assay techniques, and also

to test the effects of drugs on both standard EEG responses and on the slow potential responses.

VERNON ROWLAND, *Western Reserve University, Cleveland, Ohio.*

MY–1292. **Brain Chemistry and Behavior.**

This is a continuing program of research on the relation between brain cholinesterase (ChE) and adaptive behavior in rats. Strains of selectively bred maze-bright (Tryon $S_1$) and maze-dull (Tryon $S_3$) rats are being used. The $S_1$ rats were found to have higher brain levels of ChE than the $S_3$ animals, but cross-breeding of the two strains revealed a negative correlation between brain levels of ChE and learning capacity. More recent work—with the Tryon strains and with other genetic strains bred for high and low ChE levels—is aimed at determining whether it is the balance between acetylcholine (ACh) and ChE, rather than the ChE level alone, which is related to learning capacity. Some of the experimental procedures involve the use of drugs, including pentobarbital, strychnine, and other compounds which affect ACh or ChE. Among the many aspects of this work are studies aimed at determining the relation between ChE in red blood cells and in brain, determining the effects of training during infancy, and developing an efficient method of assaying acetylcholine from small samples of brain tissue. Histological analyses of the brain in relation to both brain chemicals and behavior are also being made.

DAVID KRECH, MARK R. ROSENZWEIG, AND EDWARD L. BENNETT, *University of California, Berkeley, Calif.*

MY–1379. **Nervous System and Behavior.**

This is a long-range, multidisciplinary program of research into the relationship of the nervous system to behavior. The effects of psychopharmacological agents and other drugs on neural function and behavior in animals, normal human subjects, and psychiatric patients are among the areas of interest.

RALPH W. GERARD, *University of Michigan, Ann Arbor, Mich.*

MY–1614. **Primary Drives and Intracranial Self-Stimulation.**

This research is aimed at localizing within the brain specific drive-reward systems involved in different basic drives and investigating the functioning of, and drug effects on, these systems. Electrodes or micropipettes permanently implanted in various areas of the brain will permit the study of electrical or pharmacological self-stimulation in relation to specific drives such as hunger, sex, or thirst, drive levels, appetite for or aversion to "drive-gratifiers" or deterrents, EEG output, and brain lesions. The experimental animals are rats.

JAMES OLDS, *University of Michigan, Ann Arbor, Mich.*

MY–1951. **Chemical Stimulation of Local Brain Areas.**

The behavioral and physiological effects of intracranial stimulation (including pharmacological and electrical self-stimulation through implanted electrodes or cannulae) are being investigated. Hormones, neural excitants and depressants, neural transmitter substances, psychotomimetics, tranquilizers, blood fractions from acute schizophrenics, operant techniques, EEG's and other procedures are being used to test hypotheses concerning neurohumoral factors in primary drive behavior. Cats, rats, and monkeys are among the experimental subjects.

ALAN E. FISHER, *University of Pittsburgh, Pittsburgh, Pa.*

MY–2004. **Chronic Brain Stimulation in Monkeys.**

This long-term program of research is concerned with the effects of chronic stimulation of the brain on behavior in cats and monkeys. Among specific areas of investigation are studies of spontaneous electrical activity, thresholds of stimulation in different points by means of permanently implanted electrodes and a timing transistor stimulator, the effects of brain stimulation on social behavior, the effects of psychopharmacological agents on brain activity and various categories of social behavior during chronic brain stimulation, and gastrointestinal changes during continuous brain stimulation.

JOSE M. R. DELGADO, *Yale University, New Haven, Conn.*

MY–2211. **Neurophysiological Response to Psychotomimetic Drugs.**

The neurophysiological actions of a variety of chemical agents which may be implicated in human psychotic behavior are being investigated in a broad program of research with animals (mainly cats and rabbits). Of particular concern is the analysis, or physiological fractionation, of the effects of serotonin on evoked potentials, in which three receptor systems—the carotid sinus area, the brain stem, and specific sensory pathways—have been discriminated. Among the compounds being studied, either separately or in terms of interactions or relation between two or more, are LSD and other psychotomimetics, noradrenaline, adrenaline, serotonin, GABA, acetylcholine, and barbiturates.

WERNER P. KOELLA AND HUDSON HOAGLAND, *Worcester Foundation for Experimental Biology, Shrewsbury, Mass.*

MY–2653. **Neural Mechanisms of Psychopharmacological Agents**

The effects of drugs, especially tranquilizers and hallucinogens, on nervous system responses to sensory input and to direct electrical stimulation will be investigated through the use of chronically implanted electrodes in

monkeys and dogs. The effects of various drugs on the threshold of stimulation of the reticular formation, diffuse thalamic projection system, posterior hypothalamus, and limbic system will be determined from EEG's. Drug effects on gross behavior and on conditioned avoidance reflexes are also being studied.

EDWARD F. DOMINO, *University of Michigan, Ann Arbor, Mich.*

MY–2754. **Biochemical Brain Changes Induced by Ataractic Drugs.**

Biochemical and metabolic studies of certain drugs (reserpine and iproniazid, for example), their effects on the central nervous system, and the effects of these drugs on the release or inhibition of serotonin and norepinephrine will be studied in mice having different degrees of genetic susceptibility to audiogenic seizures. Radioactive tracer studies may be made with labeled drugs in animals in which different parts of the brain have been removed.

RENÉ-GUY BUSNEL AND ALICE LEHMANN, *Institut National de la Recherche Agronomique, Jouy-en-Josas (Seine-&-Oise), France.*

MY–2811. **The Role of Brain Electrolytes in Drug Action.**

Experimental studies with cats are being carried out to determine whether shifts in the concentration and distribution of brain potassium play a significant role in the mode of action of certain tranquilizers and stimulants, and to what extent intrinsic variations in central potassium and calcium contribute to the relative individual effectiveness of these drugs or to the variable individual sensitivity to a particular substance. Operant conditioning techniques will be used. Electrical activity in various brain areas will be recorded through the use of chronically implanted electrodes and intraventricular cannulae implanted to permit direct central injection of drugs.

ERWIN ROY JOHN, *University of Rochester, Rochester, N.Y.*

MY–2855. **Evaluation of CNS Drugs on Rhinencephalic Activities.**

This study will explore the effects of psychotropic drugs on the rhinencephalic system and its interaction with the diencephalic and brain stem reticular mechanisms. Chronically implanted electrodes will be used to obtain data on electrical activity. The findings will be correlated with behavioral responses in experimental animals (cats and rabbits). A further aim of the study is to develop and improve neurophysiological methods of screening drugs.

BARBARA B. BROWN, *Riker Laboratories, Northridge, Calif.*

MY–2972. **Electrical Correlates of Conditioning and Perception.**

This is a study of the brain and brain processes in mediating conditioned responses. Cats will be presented with visual and auditory stimuli, and changes in electrical activity in various parts of the brain will be recorded by means of chronically implanted electrodes. The effect of drugs on electrical changes will also be observed.

ERWIN ROY JOHN, *University of Rochester, Rochester, N.Y.*

MY–3020. **Substrates for Postural Dysfunction in Schizophrenia.**

This study will investigate further the clinical observation that schizophrenic children suffer from postural and vestibular dysfunction. The clinical patterns observed in these children will be re-created in experimental animals (cats and monkeys) by means of electrical stimulation, lesions, and local drug injections. Electrical responses (in the vestibular pathways, reticular formation, and elsewhere) to stimulation of the vestibular apparatus under conditions of drug and no-drug treatment will be investigated. Vestibular stimulation will be accomplished by rotation, heating of the inner ear, and electrical stimulation. The drugs to be used include chlorpromazine, reserpine, mescaline, and LSD.

RONALD R. KOEGLER, ARNOLD B. SCHEIBEL, AND C. MARKHAM, *University of California Medical Center, Los Angeles, Calif.*

MY–3225. **Neurochemical Correlates of Behavior.**

The effects of monoamine oxidase inhibitors, 5-hydroxytryptophan and other tryptophan metabolites, serotonin antimetabolites, and possibly other chemical agents will be investigated in pigeons and monkeys in studies of the relationship between behavioral changes and increased levels of serotonin and other neurohumoral substances in discrete areas of the brain. Operant techniques are being used. Experiments designed to induce stress in the animals will also be conducted. Behavioral effects will be correlated with findings from brain assays.

MORRIS H. APRISON AND CHARLES B. FERSTER, *Indiana University, Indianapolis, Ind.*

MY–3241. **Effect of Drugs on Brain Electricity and Behavior.**

This is a program of animal experimental research in which electrophysiological, histological, and psychological techniques are being used to determine areas of electrical activity in the brain during various types of conditioned responding. An attempt will be made to determine whether different neuronal systems mediate the different kinds of responses. These methods will be used in studies of the mechanisms of action of psychopharmacological agents and other drugs. Specific techniques include the use of self-stimulation through

implanted electrodes, experimental lesions in various parts of the brain, sensory stimuli, and conditioned avoidance.

KEITH F. KILLAM, JR., *Stanford University, Stanford, Calif.*

MY–3363. **Effect on Neurohumors of Psychotogenic Procedures.**

An attempt is being made to relate changes in the brain level of biogenic amines in rats to psychotogenic procedures such as sleep deprivation and LSD administration. The tissue amine content will be altered by the administration of reserpine. LSD administration or sleep deprivation in reserpinized animals will be followed by measuring the depletion and the regeneration of biogenic amines. Standard tissue extraction methods, bio-assay procedures, and spectrophotofluorometric procedures will be used.

NICHOLAS J. GIARMAN AND DANIEL X. FREEDMAN, *Yale University, New Haven, Conn.*

MY–3374. **Drug Action on Brain Sensory and Integrative Pathways.**

This is a broad program of basic research which encompasses a number of neurophysiological and behavioral investigations of the sites and mechanisms of action of tranquilizers and antidepressives. Electrophysiological techniques will be used to study brain mechanisms of controlling sensory pathways, brain mechanisms involved in integrating incoming stimuli, and drug effects on these mechanisms.

KEITH F. KILLAM, JR., AND EVA K. KILLAM, *Stanford University, Stanford, Calif.*

MY–3477. **The Mechanism of Action of Lysergic Acid Diethylamide.**

The role of substance P (a polypeptide extractable from nervous tissue) in the nervous system will be investigated, and studies will be carried out to determine whether there is a relationship between the actions of LSD and substance P. In situ and in vitro neuropharmacological studies of modes of action will be made. Electrophysiological techniques will be used to study the actions of substance P and drugs such as LSD in the cat spinal cord. This work may be extended to include other drugs, e.g., mescaline, chlorpromazine, or reserpine.

WILLIAM A. KRIVOY, *Baylor University, Houston, Tex.*

MY–3562. **Effects of Brain Stimulation on Serotonin Release.**

Qualitative and quantitative determinations of serotonin, catecholamines, choline esters, and histamine released before, during, and after brain stimulation are to be made in dogs, cats, and rabbits. Emphasis will be on localizing the areas where these substances are released from storage or synthesized in response to the stimulation. Electric and sensory stimulation will be used. In some cases, stimulation will be induced by i.v. infusion of certain acids, bases, glucose, insulin, thyroxin, and pyrogenic solutions. The diets of some of the animals will be enriched with tryptophan and 5-hydroxytryptophan.

PETER H. BULLE, *Georgetown University, Washington, D.C.*

MY–3651. **Emotionality, Stress, and Brain Amine Levels.**

An attempt is being made to correlate brain amine levels with emotionality in rats ranked high or low in emotionality on the basis of performance on behavioral tests. Brain amine levels will also be determined before, during, or after controlled stress of varying intensity. The stress will be produced by a brief stimulus such as sound or shock, or by use of an aversive stimulus in association with or during conditioning trials. Bio-assay and chemical fluorimetric procedures, as well as tritium- and $C^{14}$-labeled intermediates of these amines, will be used.

THEODORE SCHAEFER, JR., AND JACK C. TOWNE, *University of Chicago, Chicago, Ill.*

MY–3660. **Basic Aspects of Hypothalamic "Rage."**

This research program is analyzing hypothalamic "rage" phenomena in cats from many different points of view, including physiological, endocrinological, psychological, and pharmacological approaches. It will study denervation supersensitivity and changes in the blood-brain barrier. Analysis of the aversive and/or rewarding effects of stimulating the ventromedial hypothalamic nuclei is under way, and the location of neural areas that regulate or change hypothalamic response is being attempted. It is investigating hypothalamic control of adrenal medullary secretion. Among the chemical agents being used in various aspects of the program are LSD, chlorpromazine, epinephrine, and norepinephrine.

MURRAY GLUSMAN, *New York State Psychiatric Institute, New York, N.Y.*

MY–3693. **Neuropharmacology of Audiogenic Seizures.**

The aims of this project are to classify a number of tranquilizers and antidepressives according to the effectiveness of their inhibition of sound-induced seizures in mice. The effect of escape or avoidance on mice susceptible to audiogenic seizures will be investigated, and a study made of drug effects on escape. Brain serotonin and gamma-aminobutyric acid levels during various phases of seizure will be determined, and the effects of drugs on these levels will be studied.

NICHOLAS P. PLOTNIKOFF, *Stanford Research Institute, Menlo Park, Calif.*

MY–3703. **Analysis of EEG Data in Conditioning and Drug Studies.**

Pilot studies for a data analysis and reduction system are being carried out. The purpose of the system is to facilitate EEG analyses, especially of data from chronically implanted cortical and subcortical electrodes in cats during conditioning trials and during drug-induced interference with performance.

ERWIN ROY JOHN, *University of Rochester, Rochester, N.Y.*

MY–3732. **Neural Mechanisms in Behavior.**

This is a long-term program of research which currently consists of several interrelated investigations of neural mechanisms of behavioral processes in animals and in man, including normal children. Perception, learning, and conditioning are of particular interest. The animal subjects will be monkeys.

KARL H. PRIBRAM, *Stanford University, Palo Alto, Calif.*

MY–3775. **Psychic and Motor Effects of Drugs Injected into CSF.**

This is a systematic study of catalepsy, hyperkinesia, and emotional reactions produced in unanesthetized animals (dogs, cats, and other species) through the introduction of drugs into the subarachnoid and intraventricular spaces. The effects of experimental CNS lesions, chemical agents (e.g., calcium and potassium chloride, serotonin, mescaline, rauwolfia alkaloids, hypnotics, etc.), and physical stimuli (via chronically implanted electrodes) on the induced syndromes will be investigated. Basic aims of the study are to clarify issues relating to the specificity and mechanism of action of drugs injected intracerebrally and to the physiopathology of catalepsy and certain hyperkinetic and emotional reactions.

HARRY H. GARNER AND ULRICO SACCHI, *Chicago Medical School, Chicago, Ill.*

MY–3979. **Central Mechanisms of Emotions.**

The effects of variations in frontal cortex function on fear and aggression and the effects of psychopharmacological agents (tranquilizers and antidepressives) on the thresholds of diencephalic mechanisms in fear and rage-like responses are being studied in cats. Electrical stimulation through implanted electrodes, selected drugs, and functional ablation of frontal fibers by injection of procaine will be used in carrying out this investigation. An attempt will be made to formulate more precisely the role of the frontal cortex and diencephalic areas in emotions labeled "rage," "flight," and "skulking."

WARREN W. ROBERTS, *Syracuse University, Syracuse, N.Y.*

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MY–4003. **Neurophysiology and Pharmacology of Hunger Motivation.**

The mechanisms underlying motivation for food intake are being investigated in studies of the effects of pyrogallol, iproniazid, chlorpromazine, and amphetamine on food intake in normal rats and in rats with lesions in the amygdala, ventromedial hypothalamus, and area postrema. The effects of prefeeding on drug-induced changes in food intake in the same animals will also be studied. Animals will be deprived of food for 23 hours, then the amount eaten in 30 minutes subsequent to the drug injections will be measured.

ROBERT W. REYNOLDS, *University of California, Santa Barbara, Goleta, Calif.*

MY–4035A. **Transient Exacerbation of Minimal Brain Damage.**

This is an investigation of the effects of drugs in the presence of neurological damage not severe enough to cause functional decrement. Drug effects on performance in normal rats will be compared with those occurring in rats which have minimal brain damage (i.e., not enough damage to interfere with learning). Performance levels will probably be measured by use of Hebb-Williams mazes and Lashley mazes. It is hypothesized that drugs will exacerbate the effects of brain damage. The relation between performance and chemical agent used, extent of brain damage, and area of damage will be studied, and neural histological analyses will be carried out at the end of the study.

FRANK E. HUSTMYER, JR., AND RODERICK J. SENTER. *Longview State Hospital, Cincinnati, Ohio.*

MY–4229. **Cerebral Neurohumors and Trained Behavior.**

The long-term goal of this research program is to determine the neurohumoral and biochemical changes involved in conditioned avoidance behavior with reference to providing a biochemical approach to mental disorders. Specific studies to be conducted will investigate some of the neurohumoral and biochemical factors involved in the conditioned avoidance response (CAR) and drug effects on the CAR and on the recovery of animals from electroconculsive inhibition of the CAR. Various neurohumors in certain parts of the brain during and after acquisition of the CAR will be assayed. Amines in the brain during physiopharmacological changes will be assayed by gas-phase chromatography.

CARL C. PFEIFFER, *New Jersey Neuro-Psychiatric Institute, Princeton, N.J.*

MY–4234. **Psychotomimetic Drugs and Patterns of the Auditory Cortex.**

The auditory cortical mechanisms of memory and recognition of complex sounds and speech and the effects

of drugs on these functions are being studied in dogs and monkeys. The use of 50 electrodes on the surface of cortical hearing centers will permit spatial and temporal mapping of changes in signal topology. High-speed electronic equipment is being used for rapid conversion and analysis of the resulting data. Drug effects on electrical patterns are to be investigated to determine their influence on such aspects of communication as reception, perception, and memory. The compounds to be used include LSD, GABA, chlorpromazine, adrenochrome, serotonin, and others. The work may be extended to include studies of the human cortex.

ARCHIE R. TUNTURI, *University of Oregon, Portland, Oreg.*

MY–4476A. **Effects of Drugs on the Limbic System.**

Electrophysiological studies of the sites and mechanisms of action of tranquilizers on the limbic system are being studied in cats and rabbits. Electrodes implanted in the hypothalamus, hippocampus, amygdala, and other parts of the limbic system will be used in both chronic and acute experiments. Drug effects on behavioral and EEG responses to sensory and electrical stimulation will be determined, and the actions of tranquilizers, barbiturates, and other CNS depressants will be compared.

SHOWA UEKI AND HISANOBU SUGANO, *Kyushu University, Fukuoka, Japan.*

MY–4743A. **Facts and Theories of Adrenomedullary Secretion.**

This investigator is reviewing the literature and much of his own research in various areas of neurophysiology. Papers based on the review will attempt to synthesize theories of emotion and neurohumoral integration and to relate complex physiological data to clinical problems.

E. GELLHORN, *Westmont College, Santa Barbara, Calif.*

## *Pharmacological and Biochemical Studies*

MY–388. **Electron Microscopy of the Central Nervous System.**

This project is continuing an investigation of the submicroscopic structure of the central nervous system. Attempts will be made to determine whether ultrastructural changes occur under various pathological and experimental conditions, including tranquilizing drugs, barbiturates, and other agents. The work will be done with parts of the CNS from animals and from human surgical material.

J. FRANCIS HARTMAN AND A. LAZAROW, *University of Minnesota, Minneapolis, Minn.*

MY–692. **Effects of $CO_2$ on Cerebral Circulation and Metabolism.**

This is a long-term programmatic investigation of the effects of carbon dioxide and pH upon brain and respiratory centers. An attempt is being made to determine levels of $CO_2$ vapor pressure necessary to produce depression of brain oxygen consumption, respiratory stimulation, and cerebral vasodilation in human subject. The aim of the study is to add to the knowledge of chemical mechanisms controlling respiration and the means by which pharmacological agents act upon such mechanisms.

C. J. LAMBERTSEN, *University of Pennsylvania, Philadelphia, Pa.*

MY–795. **Effects of Chemical Agents upon Cerebral Oxidation.**

This project deals with the effects of chemicals on the energy-activity correlates of neurons, and extends to local measurements of adenosinetriphosphate, disphosphopyridine nucleotide, reduced diphosphopyridine nucleotidase, and related energy-transfer substances. Effects of drugs on energy systems in specific cerebral areas are being more intensively studied by direct analyses subsequent to injections of $C^{14}$-labeled compounds.

ROBERT G. GRENELL, *University of Maryland, Baltimore, Md.*

MY–875. **Drugs and Metabolites in Epilepsy and Schizophrenia.**

A study of simple urea and other secondary amines containing carbonyl groups is under way to find the natural stimulant convulsant chemical that is blocked by anticonvulsants. Stimulant chemicals are being studied in animals (mice, cats, rats, and monkeys) and in schizophrenic patients.

HARRY L. WILLIAMS, *Emory University, Emory University, Ga.*

MY–1435. **The Effect of Tranquilizing Agents on Enzyme Systems.**

This study is based on the assumption that biochemical phenomena generally can be analyzed in terms of enzymatic reactions, and that the primary action of the tranquilizers is one of interference with enzymes. The influence of tranquilizers on the metabolism of glutamic acid, choline acetylase, carbonic anhydrase, and enzymes of glycolysis and the tricarboxylic acid cycle is being studied.

HERBERT P. JACOBI AND MICHAEL J. CARVER, *Nebraska Psychiatric Institute, Omaha, Nebr.*

MY–1841. **Enzymatic Properties of Brain Cell Fractions.**

This project will isolate pure brain mitochondria, nuclei, and microsomes by differential centrifugation and determine the structure of these components by electron and phase microscopy. It will also investigate metabolic activity of brain mitochondria and study the

effects of psychotomimetic drugs on metabolic processes of the brain.

MAGDALENA BERGER WECHSLER, *New York State Psychiatric Institute, New York, N.Y.*

MY–1902. **Humoral Agents in Cerebral Activity.**

The physiological and pharmacological aspects of substance P, a neurohumoral polypeptide implicated in CNS function, are being investigated in animals. The effects of various centrally acting drugs on substance P content of the rabbit brain and the distribution of substance P in the intestine of rats and rabbits will be studied. The effects of schizophrenic serum and hallucinogens will be measured on o-methyltransferase, diamineoxidase, histidine decarboxylase, and "substance Pase." Bio-assay procedures for these compounds will be performed on the isolated rabbit ear, hind limb of the rabbit, guinea pig ileum, and the rat uterus.

EDWARD J. WALASZEK, *University of Kansas Medical Center, Kansas City, Kans.*

MY–2263. **Effect of Tranquilizing Drugs on Tissue Metabolism.**

This is a biochemical investigation of the effects of phenothiazine-derivative tranquilizers on metabolism of muscle tissue. Studies showing that chlorpromazine and thioridazine have a pronounced metabolic effect on a viable muscle fiber preparation are being extended to include $C^{14}$-labeled substrates. The relation of high energy phosphate levels and other constituents in muscle to myographic patterns in control and pathological conditions is also being investigated. The work is being carried out with man, rats, and monkeys.

EDWARD S. WEST, RUTH D. PETERSON, AND HENRY H. DIXON, *University of Oregon, Portland, Oreg.*

MY–2338. **Metabolism of Reserpine and Related Compounds.**

Tritium-labeled reserpine and related compounds such as isoreserpine, rescinnamine, deserpidine, and others are being administered to normal and tumor-bearing mice to investigate the metabolic fate of these compounds in normal and neoplastic tissues. The enzymatic mechanisms by which these compounds are metabolized and the effects of the compounds on metabolic processes are also being investigated.

ROBERT M. BURTON, *Washington University, St. Louis, Mo.*

MY–2405. **Mechanism of Action of Ataraxic Agents.**

This project is investigating the mechanism of action of tranquilizers and barbiturates, especially the mechanism of tolerance development. Specifically, the investigators are studying the effect of phenothiazine derivatives on glutathione synthesis in liver slices from normal animals and animals made tolerant to the drugs, the distribution and metabolism of $C^{14}$-labeled meprobamate in tolerant rats, and the distribution of tritiated barbital and of $S^{35}$-labeled chlorpromazine in normal and tolerant rats. Further, an attempt will be made to determine whether decreased glutathione levels can be correlated with increased liver activity.

TOM S. MIYA, GEORGE K. W. YIM, AND J. E. CHRISTIAN, *Purdue University, Lafayette, Ind.*

MY–2435. **Studies on Brain Norepinephrine and Serotonin.**

Biochemical and pharmacological studies are being carried out to determine the properties and role of serotonin and noradrenaline in the CNS, their metabolic pathways, and the relationship between these amines and the mechanisms of action of various centrally acting drugs. The possible correlation between brain levels of serotonin and noradrenaline and CNS activity will be investigated, the behavioral changes in animals which are deficient in either of these amines will be measured and observed, and in vitro and in vivo studies of the metabolism of serotonin and noradrenaline will be caried out. The drugs to be studied include tranquilizers, psychotomimetics, and MAO inhibitors.

AKIRA HORITA, *University of Washington, Seattle, Wash.*

MY–2540. **Pharmacologic Studies of Hexafluorodiethyl Ether.**

Hexafluorodiethyl ether has been shown to elicit convulsions in many laboratory animals, and has recently been used in shock therapy in mentally disturbed patients. This work will be extended by studying the effect of other agents upon the convulsive seizure, the effect of tranquilizers on the duration and character of the seizure, and the effect of hexafluorodiethyl ether on oxygen uptake of brain tissue. It will also attempt to emulate a condition like insulin coma with hexafluorodiethyl ether, and determine the loci of its action in the brain by means of deep encephalographic electrodes.

JOHN C. KRANTZ, JR., AND EDWARD B. TRUITT, JR., *University of Maryland, Baltimore, Md.*

MY–2662. **Biogenesis of Natural Products of Medicinal Interest.**

The biogenic origins of morphine, tobacco alkaloids, rauwolfia alkaloids, mescaline, and other natural products are being investigated. The methods employed include the use of radioactively labeled precursors of these products in an attempt to isolate some of the enzyme systems responsible for synthesis of the alkaloids in plants.

EDWARD LEETE, *University of Minnesota, Minneapolis, Minn.*

MY–2717. **Role of Biogenic Amines in the Central Nervous System.**

The simultaneous metabolism and biosynthesis of biogenic amines (e.g., norepinephrine, DOPA, and dopamine) is to be studied by using a double-label technique with $C^{14}$- and tritium-labeled compounds. Storage of these amines in various tissues of untreated animals and animals receiving various drugs will be measured. Particular attention will be given to the central nervous system, and the accumulation and distribution of these amines will be measured using $H^3$- and $C^{14}$-labeled amino acid precursors of the corresponding amines, which are able to pass the blood-brain barrier. Inhibitors of enzyme systems involved in the biotransformation of these amines also will be studied.

MENEK GOLDSTEIN AND ARNOLD J. FRIEDHOFF, *New York University School of Medicine, New York, N.Y.*

MY–2927. **Factors Involved in Psychopharmacological Activity.**

This is an investigation of the relation between chemical configuration, physicochemical properties, and neuropharmacological activity of various dyes and psychopharmacologically active drugs. Affinity of these compounds and their derivatives to amino acids, peptides, and a series of proteins will be studied systematically under varied conditions.

ROLAND FISCHER AND WOLFGANG ZEMAN, *Columbus Psychiatric Institute and Hospital, Columbus, Ohio.*

MY–3231. **Monoamine Oxidases and Ganglionic Transmission.**

The effects of monoamine oxidase inhibitors on ganglionic transmission are being investigated in the cat. The superior cervical ganglion will be perfused with an MAO inhibitor, and transmission will be followed by means of electrical stimulation and recordings. Previous work has shown that several different MAO inhibitors all blocked transmission through the ganglion. The present work will attempt to clarify the nature of the block and to determine whether transmission is inhibited by a substance accumulating at the ganglionic synapse.

SHELDON B. GERTNER, *Seton Hall College of Medicine and Dentistry, Jersey City, N.J.*

MY–3271. **Pharmacologic Effects Upon Single Nerve Cell Systems.**

This is an investigation of the effect of various CNS compounds on the two Mauthner's cells in the medulla oblongata in the fish. The drugs to be studied will be administered directly into the cells or the circulatory system. Microelectrodes will be used for stimulating and recording the changes in nerve-cell activity induced by drug administration. Among the types of drugs to be used are muscle relaxants, neuromuscular blocking agents, and tranquilizers.

ERNEST RETZLAFF AND BENJAMIN PASAMANICK, *Columbus Psychiatric Institute and Hospital, Columbus, Ohio.*

MY–3319. **Biosynthesis of Psychotropic Agents in Fungi.**

The aim of this study is to isolate and identify psychotropic compounds of the indole and phenolic types. *Claviceps* (ergot), *Amanita, Agaricus* (common mushroom), and other species of fungi will be grown on synthetic media; compounds biosynthesized in this process will be tested for psychotropic activity.

HEBER W. YOUNGKEN, JR., *University of Rhode Island, Kingston, R.I.*

MY–3368. **A Study of Bio-active Secretions.**

This is a proposal to isolate and analyze the "queen substance" from secretions of queen honey bees, and to conduct controlled studies of the effects of this substance on the social behavior of bee colonies. Mammalian hormones and related substances will also be screened for effects on social behavior in bees.

ROGER A. MORSE, *Cornell University, Ithaca, N.Y.*

MY–3383. **Brain Neurohormone Levels Following CNS Stimulation.**

Quantitative determinations of levels of serotonin, norepinephrine, and acetylcholine in selected areas of the brain of rats, rabbits, or cats after nonconvulsive shock are being made in studies aimed at elucidating the biochemical basis of the effects of EST. Levels of these neurohormones will also be determined in audiogenic-seizure-susceptible rats following sound stimulation and in untreated animals.

ALBERT L. PICCHIONI AND CARL BREITNER, *University of Arizona, Tucson, Ariz.*

MY–3518. **Intermediary Metabolism and Alkaloid Biosynthesis.**

This is an investigation of the biosynthesis of ergot alkaloids in infected rye plants. Specifically, the investigator seeks to obtain information about basic metabolic pathways of the fungus by studying the action of various radioactive, Krebs cycle acids injected into the plant, and by investigating the biosynthesis of alkaloids through use of selected radioactive precursors. An attempt will be made to determine whether a change of enzymatic activity causes failure of alkaloid production when both commercially available enzymes and natural ergot enzymes are added to synthetic substrates.

GUNNAR GJERSTAD, *University of Texas, Austin, Tex.*

MY–3587. **Tryptophan in Brain Function and Mental Disease.**

Mechanisms of drug action, biochemical bases of mental illness, and the biosynthesis of diphosphopyridine nucleotide (DPN) are being investigated in studies of the changes in levels of cerebral DPN induced by tryptophan, nicotinamide, nicotinic acid, reserpine, chlorpromazine, and various combinations of these compounds. Urinary excretion of tryptophan metabolites will be measured, and fluorimetric estimations of tissue concentrations of diphosphopyridine nucleotide in the brain will be made. The work is being carried out with rats. The findings are to be compared with earlier urinary excretion studies of schizophrenics and with DPN determinations from brain biopsies of schizophrenic patients.

F. Christine Brown, *University of Tennessee, Memphis, Tenn.*

MY–3692. **Toxicity and Metabolism of Di- and Triphenylmethanes.**

The metabolism and toxicity of diphenylmethane, diphenylmethanol, benzophenone, diphenylacetic acid, benzilic acid, triphenylmethane, triphenylmethanol, and triphenylacetic acid are to be studied in rabbits and rats. Enzymatic studies of the hydroxylation of these compounds and their conjugation to glucosiduronic acids by liver preparations will be carried out. The relation between enzymatic activity and the molecular structure of the substrate will be investigated.

Herbert H. Cornish, *University of Michigan, Ann Arbor, Mich.*

MY–3694. **Protein Binding of Drugs.**

The relationship of chemical structure to protein binding will be studied by measuring the binding of a series of phenothiazine derivatives to both inert proteins and tissue homogenates. Attempts will also be made to clarify protein binding sites in studies of binding by specifically modified proteins.

Clarke Davison, *George Washington University, Washington, D.C.*

MY–3898. **Histological Correlates of Catecholamine Depletion.**

This research is concerned with the action of certain drugs on the depletion of catecholamines from the adrenal medulla and CNS of rats. Specific aims are to observe the relationship between histological changes of noradrenaline and adrenaline in the adrenal medulla and quantitative chemical changes of these substances in the brain to alterations in behavior induced by psychopharmacological compounds; to determine whether reserpine and other drugs act directly or by way of preganglionic fibers to modify the catecholamine distribution within the cromaffin cells. The unique and main aspect of the research is the development and refinement of more sensitive histochemical methods for noradrenaline conducive to its visualization in the central and sympathetic nervous system. Drugs to be studied include the monoamine oxidase inhibitors, reserpine alkaloids, antihistamines, anticholinesterase agents, the adrenolytics, and other compounds which may act as catecholamine depletors.

Ruven Greenberg, *University of Illinois, Chicago, Ill.*

MY–3903. **Physiological Influences of Psychoactive Drugs.**

This project is concerned with elucidating the mechanism of action by which certain psychopharmacological agents cause darkening (secretion and dispersal of dark pigment) in lower animals. Previous findings show the intermedin hormone of the pituitary to be involved. The present studies are to be carried out in frogs and fish by means of transplantation of the pituitary gland, brain lesions, hypophysectomy, and chemical isolation and identification of a substance producing the darkening. Also, blood samples from rats will be assayed in frogs and fish in an effort to determine the effect of drugs on the secretion of intermedin in a mammal.

George T. Scott, *Oberlin College, Oberlin, Ohio.*

MY–4008A. **Brain and Pituitary Changes Induced by Reserpine.**

The mode of action of reserpine on endocrine glands is to be investigated in histochemical studies of reserpine-induced changes in brain pituitary in rats.

Herbert Tuchmann-Duplessis, *University of Paris, Paris, France.*

MY–4295. **Pharmacology of Some Plants Indigenous to Missouri.**

The extraction, isolation, and identification of the biologically active material in ripening green walnut hulls and the bark of the black walnut tree (*Juglans nigra*), which produce "sedative" or "tranquilizing" effects in certain species of crustaceans, fish, and mammals will be attempted. Goldfish and mice will serve as subject in the bio-assay procedure in its early stages. Future investigation will be concerned with the pharmacological actions of the isolated compounds. The work will be extended to other plants (the black locust tree and the common horsetail plant) because these are considered to produce central nervous system depression in domestic animals.

Bertis A. Westfall and Robert L. Russell, *University of Missouri, Columbia, Mo.*

MY–4357. **Stabilization of Particle-Bound Neurohumors by Drugs.**

This study will attempt to elucidate the in vitro inhibitory action of psychopharmacological agents and chem-

ically related compounds on the release of acetylcholine and serotonin from their particulate form. The particles, called synaptic vesicles, will be isolated and subjected to such procedures as osmotic dilution and incubation. Following drug exposure, concentration of neurohumors will be determined by bio-assay. Preliminary results indicate that chlorpromazine inhibits the release of bound neurohumors by its effect on permeability; contributory evidence suggests that neurohumoral storage particles are identical with the synaptic vesicles.

PAUL S. GUTH, *Tulane University, New Orleans, La.*

MY–4471. **Functional Cytology—Hypothalamus and Pituitary Gland.**

The aims of this study are to delineate the cellular loci of several of the chemical constituents of the hypothalamus and pituitary gland and to provide quantitative data on these constituents. Specifically, the investigator proposes to study enzymatic properties of normal pituitary and hypothalamic tissue on an ultra-microquantitative level in rats, rabbits, and cats. The loci and magnitude of chemical changes which occur under experimental conditions (ablation, stimulation, and removal of certain endocrine glands) will be determined, and the site and mode of action of various psychotropic drugs and hormones investigated. Among the drugs to be studied are chlorpromazine, reserpine, meprobamate, lysergic acid diethylamide, amphetamine, psilocybin, salicylate, morphine, nicotine, iproniazid, and the phenethylamine hydrazides.

THADDEUS SAMORAJSKI, *Cleveland Psychiatric Institute and Hospital, Cleveland, Ohio.*

MY–4496. **Neurohormone Change Under Stimulus Deprivation.**

Neurohormone patterns and phospholipid metabolism in the brains of mice, rats, and monkeys subjected to isolation stress are to be studied. Subsequent to controlled observations, tranquilizing and other drugs which act on the central and autonomic nervous systems will be studied for their effects on behavior and neurohormone patterns accompanying isolation stress. Additional studies include the development of a technique for simultaneously separating neurohumoral substances by electrophoresis, and further investigations of the effects of phenothiazines on the incorporation of $C^{14}$ from $C^{14}$-acetate into cerebral lipids.

JENS ALLEN CHRISTENSEN, *Hahnemann Medical College, Philadelphia, Pa.*

MY–4554. **Psychoactive Drugs and Brain Nucleotides.**

This study is directed toward providing more exact knowledge of the role of free nucleotides in the functioning of the brain. The type and concentration of brain nucleotides in rabbits given injections of psychopharmacological agents (e.g., reserpine, chlorpromazine, LSD, and others) are being compared with the nucleotides in control rabbits given no drug. The brains will be frozen immediately after sacrifice of the animals in order to obtain repeatable nucleotide concentrations. Ion-exchange chromatography, paper chromatography, spectrophotometry, and other analytical methods will be used.

NAN-SING LING, *University of Michigan, Ann Arbor, Mich.*

MY–4559. **Metabolism of Aliphatic Alcohols.**

Labeled alcohols such as methanol, n-propanol, n-butanol, etc., are being studied in rat liver to determine whether during metabolism they react enzymically with malonic acid or one of its derivatives, rather than with the corresponding aldehydes and fatty acids, to yield an "aldehydogenic" compound. Previous study has shown that ethanol-l-$C^{14}$ when incubated with malonate-inhibited homogenates of rat liver yields an unidentified compound of the aldehydogenic type. The long-range aim of this work is to elucidate the role of these "aldehydogenic" compounds in the normal metabolism of alcohols in vivo.

MARTIN P. SCHULMAN, *University of Illinois, Chicago, Ill.*

MY–4578. **Metabolism of Phenothiazines.**

Investigations of the mechanism of action of the phenothiazines at the cellular and enzymatic levels will be carried out in studies of rats given isotopically-labeled phenothiazines (chlorpromazine, triflupromazine, or thioridazine). Urine, feces, and tissue will be assayed to determine metabolic fate of the drugs, localization of drugs in various tissues, and forms of the drugs in the tissues. In vitro metabolism of the labeled compounds will be studied in homogenates of various tissues. This project will also attempt comparative evaluation of the various analytical methods and techniques used in metabolic studies of the phenothiazines.

JAMES B. RAGLAND AND JOHN KINROSS-WRIGHT, *Baylor University, Houston, Tex.*

MY–4588. **Effect of Ethanol on Neurohumoral Amines.**

This is an investigation of the mode and mechanism of action by which ethanol lowers brain serotonin levels. The pharmacological and interactive role of ethanol and CNS neurohumors, particularly serotonin, will be studied in mice. In vitro and in vivo studies of the effects of ethanol on monoamine oxidase and 5-hydroxytryptophan decarboxylase will be carried out, as will measurement of urinary excretion of 5-hydroxyindole acetic acid.

BENJAMIN KISSIN AND LAURENCE S. MAYNARD, *State University of New York, Brooklyn, N.Y.*

MY–4668. **Metabolic Aspects of Mescaline Degradation.**

Mescaline metabolism and the mechanisms of mescaline's biotransformation are being studied by determining and characterizing the various metabolic products, and where feasible by investigating the pharmacological effects of the metabolites. The research includes administration of $C^{14}$-labeled mescaline. Dogs and rats are among the experimental animals being used.

ELLIOT SPECTOR, *New England College of Pharmacy, Boston, Mass.*

## *Studies of Psychotoxic Substances*

MY–2476. **Serum Protein Specificities in Mental Disorders.**

Protein patterns in normal and schizophrenic serum are being systematically investigated by producing antisera to various fractions of normal serum and the same fractions of schizophrenic serum. Special attention is being given to differences between patterns in normal and schizophrenic serum and to the possible presence of a mutated protein in the blood of schizophrenics. Heredofamilial protein relationships are also being followed.

JACQUES S. GOTTLIEB, *Lafayette Clinic, Detroit, Mich.*, AND MORRIS GOODMAN, *Wayne State University, Detroit, Mich.*

MY–2552. **Urinary Aromatic Excretion in Normals and the Mentally Ill.**

The aims of this project are to determine, by paper-chromatography techniques, the pattern of aromatic metabolites in normals, acute and chronic schizophrenics, and nonschizophrenic psychiatric patients, and to determine whether these groups metabolize ingested tryptophan in a like manner. The relationship between aromatic excretion and behavior, emotional reactions, and clinical changes will also be investigated.

MINORU MASUDA AND THOMAS H. HOLMES, *University of Washington, Seattle, Wash.*

MY–2967. ***Endogenous Psychotogens and Related* Substances.**

This is a continuation of earlier studies indicating that a factor in human blood plasma affects rats' performance on a rope-climbing test. Studies of blood plasma from normals, schizophrenics, and nonschizophrenic psychotics indicate that the substance is more active in psychotics than in normals. An attempt is being made to isolate and identify the active substance, and to determine whether it may be a metabolite which occurs in nonpsychotics during periods of emotional stress. The blood fractions are being tested in cats and rabbits for effects on electrical activity of the brain, permeability of the blood-brain barrier, and behavior.

HUDSON HOAGLAND AND JOHN R. BERGEN, *Worcester Foundation for Experimental Biology, Shrewsbury, Mass.*

MY–3690. **Behavioral and Metabolic Aspects of Indoles.**

The metabolic fate of adrenochrome, adrenolutin, and other indoles derived from adrenaline is being studied in rats, rabbits, and mice. An attempt may be made to correlate this work with studies of the findings of the cataleptic effects of these substances. Radioactive tracer techniques will be used. Since crystalline preparations of adrenochrome have not retained their properties in storage, the stability and storage characteristics of crystalline adrenochrome and adrenolutin are also being studied.

JOSEPH J. NOVAL, *Bureau of Research in Neurology and Psychiatry, Princeton, N.J.*

MY–4366A. **Schizophrenic Urine Extract Effects on Behavior and EEG.**

This study is aimed at clarifying previous findings that there are differences in the behavioral and EEG responses to schizophrenic urinary extract injected in cats intraventricularly as compared with the responses to urinary extract from nonschizophrenic subjects. The research will attempt to identify chemically the toxic substances in schizophrenic urine and to develop better behavioral measures of the animals' responses. Work will also be extended to other animals, particularly mice, in the hopes of making it possible to do large-scale screening.

SHIGEO FUJITA, *Ypsilanti State Hospital, Ypsilanti, Mich.*

## SYNTHESIS OF PSYCHOPHARMACOLOGICAL AGENTS

MY–1239. **Benzophenothiazines as Chemotherapeutic Agents.**

A number of N-dialkylaminoalkyl-benzophenothiazines related to currently used phenothiazine derivatives are being synthesized and evaluated pharmacologically.

DAVID A. SHIRLEY, *University of Tennessee, Knoxville, Tenn.*

MY–1301. ***Bioactive Indole Compounds.***

Indoles and oxindoles of the serotonin and bufotenine type are being synthesized with a view toward improving and simplifying methods of synthesizing such compounds, increasing the number of useful therapeutic agents, and revealing further information about the biosynthesis of indole compounds in plants. Theories concerning the

biosynthesis of indole alkaloids are being tested by carbon tracer techniques and in vitro experiments.

ERNEST WENKERT, *Iowa State College, Ames, Iowa.*

MY–1588. **Chemical Structure and Psychotomimetic Activity.**

In a continuing study of the relationship between chemical structure and psychotomimetic activity, a number of substituted phenylalkylamines and indoles are being synthesized and examined. Correlative studies of the neurophysiological, gross behavioral, and biochemical (enzymatic) effects of the compounds are being carried out with animals, mainly cats at present.

RICHARD D. MORIN AND F. BENINGTON, *Battelle Memorial Institute, Columbus, Ohio.*

MY–2029. **Studies with 4-Substituted Indoles.**

A number of new compounds related to reserpine and lysergic acid diethylamide have been synthesized, and their pharmacological properties investigated in animals. This aspect of the study will continue synthetic chemical work with 4-substituted indoles with a view to preparing compounds based upon the tetrahydrobenzindole ring system. The long-range goal is the total synthesis of the ergoline ring system. Pharmacological studies are also being continued.

FREDERICK C. UHLE, *Harvard University, Cambridge, Mass.*

*MY–2037.* ***Indole Derivatives of Medicinal Interest.***

The purpose of this project is to synthesize spirooxindoles and related indolines structurally related to the mitragyna alkaloids, to prepare analogues of the iboga alkaloids, and to investigate their pharmacological properties. Methods for the total synthesis of these products are to be developed. The relation of structure to psychopharmacological activity in animals will be investigated.

FRANCIS M. MILLER, *University of Maryland, Baltimore, Md.*

MY–2072. **Molecular Structure and Enzymodynamic Properties.**

A number of compounds related to organic amines will be synthesized. Their effects upon enzymes involved in brain metabolism will be studied to determine structure-activity relationships.

ANDREW LASSLO AND JAMES A. BAIN, *Emory University, Emory University, Ga.*

MY–2756. **Synthesis of Psychopharmacological Compounds.**

These investigators are developing synthesis techniques and exploring various preparative routes for obtaining compounds of psychopharmacological interest. A number of 7-hydroxyindole bases and two or three methylated tryptophan derivatives are being prepared. In addition, methylated epinephrine analogues are being synthesized.

EARL USDIN AND ROBERT BECKER, *New Mexico Highlands University, Las Vegas, N. Mex.*

MY–2799. **Synthesis of Benzilic Acid Derivatives.**

Esters of benzilic acid are being prepared with amino alcohols and tested pharmacologically for antispasmodic and CNS activity. Structures will be correlated with CNS activity.

JOSEPH G. CANNON, *University of Wisconsin, Madison, Wis.*

MY–3232. **Open Chain Analogues of Reserpine.**

Two new types of open-chain analogues of reserpine are to be synthesized by employing the Mannich reaction. The pharmacological properties of the synthesized compounds will be compared with those of reserpine.

W. LEWIS NOBLES, *University of Mississippi, University, Miss.*

MY–3273. **Synthesis of Psychochemical Agents.**

An attempt is being made to synthesize compounds related to β-phenylethylamine, phenylalanine, and indole, incorporating the essential structural features of the epinephrines and mescaline. Psychopharmacological studies will then be carried out to determine the relation of chemical structure to activity.

ORRIE M. FRIEDMAN, *Brandeis University, Waltham, Mass.*

MY–3665. **The Effect of Psychoactive Agents on Brain and Behavior.**

This investigation of the structure-activity relationships of drugs which affect the central nervous system will include the synthesis of new compounds whose neuropharmacological properties will be compared with those of known psychotherapeutic drugs. The effects of modifications in the shape and size of certain molecules will be tested in physiological and behavioral studies of cats, rats, and monkeys.

ROBERT G. GRENELL, *University of Maryland, Baltimore, Md.*

MY–3930. **Synthesis of Some Substituted β-Lactams.**

Several new types of substituted β-lactams and γ-lactams belonging to the barbiturate and thiobarbiturate group of compounds are being synthesized and evaluated for physiological and CNS activity. β-lactams substituted with amino acid residue, halogen, carboxy, mercapto, and amino groups or their derivatives may also be synthesized. This project was prompted by findings

indicating that certain substituted β-lactams and γ-lactams possess powerful hypnotic and sedative properties.

AJAY K. BOSE, *Stevens Institute of Technology, Hoboken, N.J.*

MY–4132. **The Synthesis of CNS Active Trimethoxyphenyl Analogues.**

A series of 3,4,5-trimethoxyphenyl compounds similar to drugs with known CNS activity are to be synthesized and screened for pharmacological properties with emphasis on psychotropic properties and antimitotic activity. Attention will be given to the specificity and importance of the trimethoxyphenyl moiety in compounds possessing psychotropic activity.

PIERRE F. SMITH AND JOHN J. DEFEO, *University of Rhode Island, Kingston, R.I.*

MY–4582. **Synthesis of Compounds Related to Lysergic Acid.**

Compounds structurally related to lysergic acid are to be synthesized. Relation between molecular structure and LSD-like activity of the new compounds will then be investigated.

JOHN C. CRAIG, *University of California Medical Center, San Franciso, Calif.*

## METHOD DEVELOPMENT

MY–788. **Studies of Autonomic Response Patterns.**

The major aims of this research are to explore and refine techniques for measuring and statistically analyzing autonomic response patterns in man, and to continue investigating the autonomic response patterns to a variety of physical and psychological stimuli, the value of these patterns in predicting response to stress, and the relationship of autonomic response patterns to personality. The investigator is also testing the hypothesis that emotional behavior in man is characterized by at least eight fundamentally different autonomic response patterns.

M. A. WENGER, *University of California, Los Angeles, Calif.*

MY–2950. **Human Psychophysiology Research Methodology.**

The aims of this project are to test the value and practicability of using a high-speed data recording and processing system to record simultaneously a number of physiological and behavioral variables. Regression equations and sets of partial differential equations are to be constructed for use in describing and predicting psychophysiological states, and for logically describing the dynamic systems involved in the psychophysiological processes. This work will be carried out with normals and with hospitalized psychiatric patients. One of the experimental conditions involves the administration of epinephrine, norepinephrine, or methacholine.

ALBERT F. AX, *Lafayette Clinic, Detroit, Mich.*

MY–3008. **Assessment Methods for Psychopharmacological Research.**

The Wittenborn Psychiatric Rating Scale, which was originally designed for use in describing newly admitted mental hospital patients, is being extended to include the behavior of chronic schizophrenics, deteriorated patients, and patients being treated with tranquilizers. Also, an interview procedure for studying drug-induced or other changes in psychiatric patients is being cross-validated and standardized. The interview studies are being carried out with normals, a heterogeneous group of hospitalized patients, and a group of depressed, nonschizophrenic patients.

J(OHN) RICHARD WITTENBORN, *Rutgers University, New Brunswick, N.J.*

MY–3262. **An Inventory of Psychiatric Patient Behavior.**

Two behavior inventories to measure symptoms and interpersonal reactions in psychiatric patients are to be constructed and tested, one for use with psychotics and the other for use with psychoneurotics. Tests of reliability and validity of the inventories are to be carried out. Data are also being collected for developing interview patterns for use with the inventories.

JAMES P. O'CONNOR AND MAURICE LORR, *Catholic University of America, Washington, D.C.*

MY–4233. **Rater Perseveration in Measures of Patient Change.**

The aims of this investigation are to determine whether ratings of drug-treated patients are prematurely stereotyped when the same rater(s) makes successive ratings of the patients, and thus whether an artifact is introduced which influences evaluations of treatment changes. These questions will be examined in a study in which the Lorr Multidimensional Scale for Rating Psychiatric Patients and a revised form of that scale, the Inpatient Multidimensional Psychiatric Scale, will be used to rate changes in hospitalized psychiatric patients who are the subjects of a comparative evaluation of several phenothiazines.

MARY H. TATOM AND THOMAS E. HANLON, *Spring Grove State Hospital, Baltimore, Md.*

MY–4664. **Sound Oscillographic Patterns in Psychopathology.**

A major aim of this project is to establish an objective method for evaluating behavior through studies of the effects of drugs, stress, and EST on vocalization patterns.

Data on quality of vocalization (e.g., intensity, modulation, frequency, and rate and rhythm) will be correlated with clinical judgments of mood, affect, and tension in schizophrenics, patients with severe CNS disease, and subjects free of neuropsychiatric disorders. Specially constructed sound recording and amplifying instruments will be used to analyze characteristics of both spontaneous and directed speech.

ARNOLD J. FRIEDHOFF AND MURRAY ALPERT, *New York University Medical Center, New York, N.Y.*

## SCIENTIFIC INFORMATION IN PSYCHOPHARMACOLOGY

MY–2679. **Translation and Review of Russian Psychiatric Literature.**

The Russian literature in the following areas of psychiatry is being translated and systematically reviewed: Soviet psychotherapy and treatment of neuroses, schizophrenia and other major psychoses, mental retardation and rehabilitation techniques, experimental clinical work, and psychopharmacology.

JOSEPH WORTIS, *152 Hicks Street, Brooklyn, N.Y.*

3M–9163. **Translation of Articles in Psychopharmacology.**

Selected psychopharmacological papers in foreign languages are being translated into English and in some cases are being abstracted. The work is being carried out in cooperation with the Scientific Information Unit of the Psychopharmacology Service Center.

CHARLOTTE WALDO AND NATHAN S. KLINE, *Rockland State Hospital, Orangeburg, N.Y.*

3M–9170. **Bibliographic Research in Psychopharmacology.**

This project involves the preparation of several special annotated bibliographies in the field of psychopharmacology.

MIRIAM R. GELLER, *Massachusetts Mental Health Research Center, Boston, Mass.*

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